

# BMJ Best Practice

## Coronavirus disease 2019 (COVID-19)

Straight to the point of care



Last updated: Sep 29, 2020

# Table of Contents

<b>Summary</b>	<b>3</b>
<b>Basics</b>	<b>4</b>
Definition	4
Epidemiology	4
Etiology	5
Pathophysiology	9
Classification	10
<b>Prevention</b>	<b>13</b>
Primary prevention	13
Screening	18
<b>Diagnosis</b>	<b>20</b>
Case history	20
Step-by-step diagnostic approach	20
Risk factors	32
History & examination factors	40
Diagnostic tests	43
Differential diagnosis	50
Diagnostic criteria	53
<b>Treatment</b>	<b>54</b>
Step-by-step treatment approach	54
Treatment details overview	69
Treatment options	72
Emerging	98
<b>Follow up</b>	<b>104</b>
Recommendations	104
Complications	107
Prognosis	114
<b>Guidelines</b>	<b>119</b>
Diagnostic guidelines	120
Treatment guidelines	122
<b>Online resources</b>	<b>127</b>
<b>References</b>	<b>131</b>
<b>Images</b>	<b>193</b>
<b>Disclaimer</b>	<b>194</b>

## Summary

- ◇ Coronavirus disease 2019 (COVID-19) is an infectious acute respiratory disease caused by a novel coronavirus. The World Health Organization (WHO) was informed of cases of pneumonia of unknown microbial etiology associated with Wuhan City, Hubei Province, China on 31 December 2019. The WHO later announced that a novel coronavirus had been detected in samples taken from these patients. Since then, the epidemic has escalated and rapidly spread around the world, with the WHO first declaring a public health emergency of international concern on 30 January 2020, and then formally declaring it a pandemic on 11 March 2020. Clinical trials and investigations to learn more about the virus, its origin, how it affects humans, and its management are ongoing.
-

## Definition

A potentially severe acute respiratory infection caused by the novel coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] The clinical presentation is generally that of a respiratory infection with a symptom severity ranging from a mild common cold-like illness, to a severe viral pneumonia leading to acute respiratory distress syndrome that is potentially fatal. Characteristic symptoms include fever, cough, and dyspnea, although some patients may be asymptomatic. Complications of severe disease include, but are not limited to, multi-organ failure, septic shock, and venous thromboembolism.

## Epidemiology

### Adults

- In China, 87% of confirmed cases were ages 30 to 79 years and 3% were ages 80 years or older. Approximately 51% of patients were male.[4]
- In Italy, the median age and prevalence of comorbidities was higher compared with China.[5]
- In the UK, the median age of patients was 73 years and males accounted for 60% of admissions in a prospective observational cohort study of more than 20,000 hospitalized patients.[6]
- In the US, older patients (ages  $\geq 65$  years) accounted for 31% of all cases, 45% of hospitalizations, 53% of intensive care unit admissions, and 80% of deaths, with the highest incidence of severe outcomes in patients ages  $\geq 85$  years.[7]

### Children

- Children are less likely to be affected than adults, and account for a low proportion of confirmed cases depending on geographic location:[4] [8] [9] [10] [11] [12] [13]
  - China - 2.1% (median age 7 years)
  - Italy - 1.2% (median age 4 to 5 years; higher in males but not statistically significant)
  - Spain - 0.8% (median age 3 years)
  - US - 10.3% (or 780 cases per 100,000 children in the population) as of 17 September.
  - [American Academy of Pediatrics: children and COVID-19 – state-level data report]
- In the UK, a prospective observational cohort study found that children and young adults represented 0.9% of all hospitalized patients at the time. The median age of children admitted to hospital was 4.6 years, 56% were male, 35% were under 12 months of age, and 42% had at least one comorbidity. In terms of ethnicity, 57% were White, 12% were South Asian, and 10% were Black. Age under 1 month, age 10 to 14 years, and Black race were risk factors for admission to critical care.[14]
- Most cases are from familial clusters, or children who have a history of close contact with an infected patient.[15] It appears that children generally don't spread the virus to household contacts.[16] Unlike adults, children do not seem to be at higher risk for severe illness based on age or sex.[17]

### Pregnant women

- A meta-analysis of over 2500 pregnant women with confirmed COVID-19 found that 73.9% of women were in the third trimester; 50.8% were from Black, Asian, or minority ethnic groups; 38.2% were obese; and 32.5% had chronic comorbidities.[18]
- In the UK, the estimated incidence of admission to hospital with confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in pregnancy is 4.9 per 1000 maternities. Most

women were in the second or third trimester. Of these patients, 41% were ages 35 years or older, 56% were from Black or other ethnic minority groups, 69% were overweight or obese, and 34% had preexisting comorbidities.[19]

- In the US, according to an analysis of 8200 infected pregnant women, Hispanic and non-Hispanic Black pregnant women appear to be disproportionately affected during pregnancy.[20]

#### Healthcare workers

- The overall proportion of healthcare workers who tested positive for SARS-CoV-2 among all patients with COVID-19 in a living systematic review and meta-analysis was 11% via polymerase chain reaction, and 7% via antibody screening. The most frequently affected healthcare workers were nurses. Only 5% of healthcare workers developed severe disease and 0.5% died.[21] The incidence of severe or critical disease and mortality in healthcare workers was lower than the incidence of severe or critical disease and mortality in all patients.[22]
- Infection rates in healthcare workers vary according to location:[22] [23] [24]
  - US - 18%
  - UK - 10%
  - Italy - 9%
  - Netherlands - 6%
  - China - 4.2%.
- The majority of healthcare workers with COVID-19 reported contact in the healthcare setting. In a study of over 9000 cases reported in healthcare workers in the US, 55% had contact only in a healthcare setting, 27% only in a household, 13% only in the community, and 5% in more than one setting.[25]

#### Resources

- [\[WHO: coronavirus disease \(COVID-19\) emergency dashboard\]](#)
- [\[WHO: coronavirus disease \(COVID-2019\) weekly epidemiological updates\]](#)
- [\[CDC: COVIDView\]](#)

## Etiology

### Virology

- Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a previously unknown betacoronavirus that was discovered in bronchoalveolar lavage samples taken from clusters of patients who presented with pneumonia of unknown cause in Wuhan City, Hubei Province, China, in December 2019.[26]
- Coronaviruses are a large family of enveloped RNA viruses, some of which cause illness in people (e.g., common cold, severe acute respiratory syndrome [SARS], Middle East respiratory syndrome [MERS]), and others that circulate among mammals and birds. Rarely, animal coronaviruses can spread to humans and subsequently spread between people, as was the case with SARS and MERS.
- SARS-CoV-2 belongs to the *Sarbecovirus* subgenus of the *Coronaviridae* family, and is the seventh coronavirus known to infect humans. The virus has been found to be similar to SARS-like

coronaviruses from bats, but it is distinct from SARS-CoV and MERS-CoV.[27] [28] The full genome has been determined and published in GenBank. [GenBank]

- A preliminary study suggests that there are two major types (or strains) of the SARS-CoV-2 virus in China, designated L and S. The L type was found to be more prevalent during the early stages of the outbreak in Wuhan City and may be more aggressive (although this is speculative), but its frequency decreased after early January. The relevance of this finding is unknown at this stage and further research is required.[29] Patients in Singapore infected with a SARS-CoV-2 variant with a 382-nucleotide deletion appeared to have a milder course compared with those infected with a wild-type virus.[30]

#### [Fig-1]

#### Origin of virus

- A majority of patients in the initial stages of this outbreak reported a link to the Huanan South China Seafood Market, a live animal or "wet" market, suggesting a zoonotic origin of the virus.[31] [32] [33] An initial assessment of the transmission dynamics in the first 425 confirmed cases found that 55% of cases before 1 January 2020 were linked to the market, whereas only 8.6% of cases after this date were linked to the market. This suggests that person-to-person spread was occurring among close contacts since the middle of December 2019.[33]
- Some studies suggest that SARS-CoV-2 may be a recombinant virus between a bat coronavirus and an origin-unknown coronavirus.[27] [28] [34] [35] Pangolins have been suggested as a possible intermediate host; however, the virus has not been identified in an animal host as yet.[36] [37] [38] Further research is required to determine the origin of SARS-CoV-2.

#### Transmission dynamics

- Respiratory transmission is the dominant mode of transmission, with proximity and ventilation being the key determinants of transmission risk.[39] Available evidence suggests that transmission between people occurs primarily through direct, indirect, or close contact with infected people through infected secretions such as saliva and respiratory secretions, or through their respiratory droplets, which are expelled when an infected person coughs, sneezes, talks, or sings.[40]
- Airborne transmission can occur in healthcare settings during aerosol-generating procedures. There are some outbreak reports that suggest aerosol transmission is possible in the community; however, these reports relate to indoor crowded spaces with poor ventilation (e.g., restaurants, choir practice, fitness classes), and a detailed investigation of these clusters suggests that droplet and fomite transmission could also explain the transmission in these reports.[40]
- Fomite transmission (from direct contact with fomites) may be possible, but there is currently no conclusive evidence for this mode of transmission. In the few cases where fomite transmission has been presumed, respiratory transmission has not been completely excluded.[39] The virus has been found to be more stable on plastic and stainless steel (up to 72 hours) compared with copper (up to 4 hours) and cardboard (up to 24 hours) under experimental conditions.[41] In healthcare settings, the virus is widely distributed in the air and on object surfaces in both general wards and intensive care units.[42] However, no virus has been cultured from these samples indicating that the deposition may reflect nonviable viral RNA.[43]
- Fecal-oral transmission (or respiratory transmission through aerosolized feces) may be possible, but there is only limited circumstantial evidence to support this mode of transmission.[39] The pooled detection rate of fecal SARS-CoV-2 RNA in patients with COVID-19 is approximately 51%, with 64%

of samples remaining positive for a mean of 12.5 days (up to 33 days maximum) after respiratory samples became negative.[44]

- Transmission via other body fluids (including sexual transmission or bloodborne transmission) has not been reported.[39] While the virus has been detected in blood, cerebrospinal fluid, pericardial fluid, pleural fluid, urine, semen, saliva, tears, and conjunctival secretions, as well as in the middle ear and mastoid, the presence of virus or viral components does not equate with infectivity.[45] [46] [47] [48] [49] [50] [51] [52] [53] [54] [55]
- Vertical transmission occurs rarely and transplacental transmission has been documented.[39] Vertical transmission has been reported in approximately 3.2% of patients, usually in the third trimester.[56] The rate of infection appears to be no greater when the baby is born vaginally, breastfed, or allowed contact with the mother.[57] Viral fragments have been detected in breast milk; however, no replication-competent virus has been detected, suggesting that transmission via breast milk is unlikely.[58] [59] [60] Vertical transmission is unlikely to occur if correct hygiene precautions are taken.[61]
- Nosocomial transmission was reported in 44% of patients in one systematic review; however, this review was limited to case series conducted early in the outbreak in Wuhan before the institution of appropriate infection prevention and control measures.[62] The nosocomial infection rate in a major London teaching hospital was around 15% during the peak of the outbreak.[63] More recent reports of healthcare workers exposed to index cases (not in the presence of aerosol-generating procedures) found little to no nosocomial transmission when contact and droplet precautions were used.[40] [64]

#### Transmission dynamics in relation to symptoms

- Symptomatic transmission
  - Transmission appears to be greatest when people are symptomatic, especially around the time of symptom onset.[2] [65] [66] [67] [68] [69] [70] [71]
- Presymptomatic transmission
  - Transmission may occur during the incubation period, usually 1 to 3 days before symptom onset.[2]
  - Presymptomatic transmission was reported in 12.6% of cases in China, and 6.4% of cases in Singapore.[72] [73]
  - People without symptoms may be presymptomatic, or they may remain persistently asymptomatic.
- Asymptomatic transmission
  - Transmission from asymptomatic cases (laboratory-confirmed cases who do not develop symptoms) has been documented.[74] [75] However, evidence is limited, and the World Health Organization states that asymptomatic cases are much less likely to transmit the virus than those who develop symptoms, and asymptomatic cases are not the major driver of the overall epidemic dynamics.[76] [77] Numerous studies have reported no evidence of asymptomatic transmission from carriers of SARS-CoV-2.[78] [79] [80]
  - Estimating the prevalence of asymptomatic cases in the population is difficult. A meta-analysis of over 50,000 people found that 15.6% of confirmed cases were asymptomatic at the time of testing, and nearly half developed symptoms later.[81] However, estimates of the proportion of asymptomatic cases vary widely from between 1.2% to 80%, depending on the study population.[82] [83] [84] [85] [86] [87] [88]

- Healthcare workers may play a role in asymptomatic transmission. About 7.6% of healthcare workers who worked in hospital units with infected patients tested positive for SARS-CoV-2 antibodies; however, only 58% of these workers reported prior symptoms.[89] A cross-sectional study of nearly 2800 healthcare workers found that 5.4% of COVID-19-facing asymptomatic healthcare workers tested positive, compared with 0.6% of non-COVID-19-facing asymptomatic healthcare workers.[90]
- Children are more likely to be asymptomatic.[81] The pooled proportion of asymptomatic cases in children was thought to be significant (around 40%).[91] [92] However, a recent study found that the rate of asymptomatic infection in children was 1% compared with 9% in adults.[93]

#### Superspreading events

- Superspreading events have been reported. These events are associated with explosive growth early in an outbreak and sustained transmission in later stages.[94]
- Reported events include church/religious gatherings, weddings, choir practices, overnight youth camps, fitness classes, business conferences, and working in call centers.[39] Widespread transmission has also been reported in long-term care facilities, homeless shelters, prisons, and meat and poultry processing facilities, as well as on board cruise ships.[95] [96] [97] [98] [99] [100] [101] There is a lack of evidence for transmission in the school setting.[102]
- Some individuals are supershedders of virus, but the reasons underlying superspreader events are often more complex than just excess virus shedding and can include a variety of behavioral, host, and environmental factors.[103]

#### Viral transmission factors

- Incubation period
  - The incubation period is estimated to be between 1 and 14 days, with a median of 5 to 6 days.[2] [104] Infectiousness peaks around 1 day before symptom onset and declines within 7 days.[39]
- Reproduction number ( $R_0$ )
  - Preliminary reports suggested that the reproduction number, the number of people who acquire the infection from an infected person, was estimated to be 2.2 to 3.3.[33] [105] [106] The Centers for Disease Control and Prevention gives a current best estimate of 2.5 (as of 10 September 2020).[107]
  - The  $R_0$  decreases when public health measures (e.g., social distancing) are put in place.[108]
- Secondary attack rate
  - The secondary attack rate, the proportion of people exposed to a primary case that go on to develop the disease as a result of the exposure, among all close contacts ranges from 0.45% to 3.7%. The rate among household members, particularly spouses, is higher and ranges from 4.6% to 30%. The rate lowered to 0% when index patients were quarantined by themselves from the onset of symptoms.[76] [109] [110] [111] [112]
  - The secondary attack rate increases with the severity of the index case (i.e., 0.3% for asymptomatic cases to 6.2% for severe/critical cases) according to a study of 3410 close contacts of 391 index cases.[76]

- The secondary attack rate for close contacts of presymptomatic people is approximately 3.3%, with a rate of 16.1% for household contacts, 1.1% for social contacts, and 0% for work contacts.[113]
- Children ages <5 years had lower secondary attack rates compared with older children, and the risk of infection was higher if the household index case was the mother.[114] The secondary attack rate was 1.2% in children in a childcare setting or school.[115]
- Viral load
  - Viral load is highest in the upper respiratory tract (nasopharynx and oropharynx) early in the course of infection, and then increases in the lower respiratory tract (sputum). Viral load rapidly decreases after symptom onset. Patients with severe disease have higher viral loads compared with those with mild disease.[39]
  - Viral load in the upper respiratory tract is comparable in asymptomatic patients and those with mild symptoms.[116]
- Viral shedding
  - The median duration of viral shedding has been estimated to be between 8 and 20 days after symptoms resolve. However, shedding has been detected for up to 60 days in various samples, and for 104 days in one pregnant woman.[117] [118] [119] [120] [121] [122] [123]
  - Duration of viral shedding was longer in symptomatic patients compared with asymptomatic patients (25.2 days versus 22.6 days), and in patients with severe illness compared with those with mild illness (21 days versus 14 days).[124] [125]
  - The period of infectiousness is far shorter than the duration of detectable viral shedding. No viable virus has been isolated in patients with mild or moderate disease after 10 days of symptoms, or after 20 days in those with severe or critical disease, despite ongoing viral shedding. Data about the dynamics of viral shedding in people with persistent asymptomatic infection are inconsistent.[39] There is no convincing evidence that duration of viral shedding correlates with duration of infectivity.[126]
  - Factors associated with prolonged viral shedding include male sex, older age, comorbid hypertension, delayed admission to hospital after symptom onset or severe illness on admission, and use of invasive mechanical ventilation or corticosteroids.[127]

## Pathophysiology

The pathophysiology of COVID-19 is not fully understood; however, it has been confirmed that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) binds to the angiotensin-converting enzyme-2 (ACE2) receptor in humans, which suggests a similar pathogenesis to SARS.[28] [128] A unique structural feature of the spike glycoprotein receptor binding domain of SARS-CoV-2 (which is responsible for the entry of the virus into host cells) confers potentially higher binding affinity for ACE2 on host cells compared with SARS-CoV.[129] Mechanistic evidence from other coronaviruses suggests that SARS-CoV-2 may downregulate ACE2, leading to a toxic overaccumulation of plasma angiotensin-II, which may induce acute respiratory distress syndrome and fulminant myocarditis.[130] [131]

Based on an analysis of single-cell RNA sequencing datasets derived from major human physiologic systems, the organs considered more vulnerable to SARS-CoV-2 infection due to their ACE2 expression levels include the lungs, heart, esophagus, kidneys, bladder, and ileum.[132] This may explain the extrapulmonary manifestations associated with infection. Lower expression of ACE2 in the nasal epithelium

of children ages <10 years compared with adults may explain why COVID-19 is less prevalent in children; however, further research on this is required.[133]

The virus uses the host transmembrane protease serine 2 (TMPRSS2) for S protein priming and fusion of viral and host cell membranes.[134] Higher expression of TMPRSS2 has been noted in the nasal epithelium of Black people compared with Asian people, Latin people, White people, and people of mixed race/ethnicity, which may be a contributing factor to the higher burden of infection among Black people.[135]

A furin-like cleavage site has been identified in the spike protein of the virus; this does not exist in other SARS-like coronaviruses.[136]

Autopsy studies have revealed that patients who died of respiratory failure had evidence of exudative diffuse alveolar damage with massive capillary congestion, often accompanied by microthrombi. Hyaline membrane formation and pneumocyte atypical hyperplasia are common. Pulmonary artery obstruction by thrombotic material at both the macroscopic and microscopic levels has been identified. Patients also had signs of generalized thrombotic microangiopathy. Severe endothelial injury associated with the presence of intracellular virus and disrupted cell membranes has been noted. Other findings include bronchopneumonia, pulmonary embolism, alveolar hemorrhage, and vasculitis. Significant new blood vessel growth through intussusceptive angiogenesis distinguishes the pulmonary pathology of COVID-19 from severe influenza infection.[137] [138] [139] [140] [141] [142]

Histopathologic examination of brain specimens showed hypoxic changes but no encephalitis or other specific brain changes due to the virus in one autopsy study. The virus was detected at low levels in brain tissue.[143]

SARS-CoV-2 has been frequently detected in the myocardium in autopsy studies.[144] The virus, along with inflammatory changes, has been reported in the cardiac tissue of a child with pediatric inflammatory multisystem syndrome.[145]

Other novel findings at autopsy include pancreatitis, pericarditis, adrenal microinfarction, secondary disseminated mucormycosis, and brain microglial activation.[146]

There is a hypothesis that COVID-19 is a disease of the endothelium.[147] [148] [149] Endotheliopathy and platelet activation appear to be important features of COVID-19 in hospitalized patients and are likely to be associated with coagulopathy, critical illness, and death.[150] Hyperviscosity has been reported in patients. It is known to damage the endothelium, and is a known risk factor for thrombosis. The potential link between hyperviscosity and thrombotic complications warrants further investigation.[151]

Genetic factors are thought to play a role in the pathogenesis. In a case series of four male patients with severe disease, rare putative loss-of-function variants of X-chromosomal TLR7 were identified, and this was associated with impairment of interferon responses.[152]

## Classification

### World Health Organization: COVID-19 disease severity[2]

Mild illness

- Symptomatic patients meeting the case definition for COVID-19 without evidence of hypoxia or pneumonia.
- Common symptoms include fever, cough, fatigue, anorexia, dyspnea, and myalgia. Other nonspecific symptoms include sore throat, nasal congestion, headache, diarrhea, nausea/vomiting, and loss of smell/taste.
- Older people and immunosuppressed people may present with atypical symptoms (e.g., fatigue, reduced alertness, reduced mobility, diarrhea, loss of appetite, delirium, absence of fever).
- Symptoms due to physiologic adaptations of pregnancy or adverse pregnancy events (e.g., dyspnea, fever, gastrointestinal symptoms, fatigue) or other diseases (e.g., malaria) may overlap with COVID-19 symptoms.

#### Moderate disease

- Adolescent or adult: clinical signs of pneumonia (i.e., fever, cough, dyspnea, fast breathing) but no signs of severe pneumonia, including blood oxygen saturation levels ( $\text{SpO}_2$ )  $\geq 90\%$  on room air.
- Children: clinical signs of nonsevere pneumonia (i.e., cough or difficulty breathing plus fast breathing and/or chest indrawing) and no signs of severe pneumonia. Fast breathing is defined as:
  - <2 months of age:  $\geq 60$  breaths/minute
  - 2-11 months of age:  $\geq 50$  breaths/minute
  - 1-5 years of age:  $\geq 40$  breaths/minute.
- While the diagnosis can be made on clinical grounds, chest imaging may assist in diagnosis and identify or exclude pulmonary complications.

#### Severe disease

- Adolescent or adult: clinical signs of pneumonia (i.e., fever, cough, dyspnea, fast breathing) plus one of the following:
  - Respiratory rate  $>30$  breaths/minute
  - Severe respiratory distress
  - $\text{SpO}_2 < 90\%$  on room air.
- Children: clinical signs of pneumonia (i.e., cough or difficulty in breathing) plus at least one of the following:
  - Central cyanosis or  $\text{SpO}_2 < 90\%$
  - Severe respiratory distress (e.g., fast breathing, grunting, very severe chest indrawing)
  - General danger sign
  - Inability to breastfeed or drink, lethargy or unconsciousness, or convulsions.
- While the diagnosis can be made on clinical grounds, chest imaging may assist in diagnosis and identify or exclude pulmonary complications.

#### Critical disease

- Presence of acute respiratory distress syndrome (ARDS), sepsis, or septic shock.
- Other complications include acute pulmonary embolism, acute coronary syndrome, acute stroke, and delirium.

## National Institutes of Health: clinical classification of COVID-19<sup>[3]</sup>

### Asymptomatic or presymptomatic infection

- People who test positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) but have no symptoms.

### Mild illness

- People who have any of various signs and symptoms (e.g., fever, cough, sore throat, malaise, headache, muscle pain) without shortness of breath, dyspnea, or abnormal imaging.

### Moderate illness

- People who have evidence of lower respiratory disease by clinical assessment or imaging and an oxygen saturation ( $\text{SpO}_2$ )  $>93\%$  on room air at sea level.

### Severe illness

- People who have respiratory frequency  $>30$  breaths per minute,  $\text{SpO}_2 \leq 93\%$  on room air at sea level, ratio of arterial partial pressure of oxygen to fraction of inspired oxygen ( $\text{PaO}_2/\text{FiO}_2$ )  $<300$ , or lung infiltrates  $>50\%$ .

### Critical illness

- People who have respiratory failure, septic shock, and/or multiple organ dysfunction.

# Primary prevention

## Infection prevention and control for healthcare professionals

- Always consult local infection prevention and control protocols; only basic principles are detailed here.
- Immediately isolate all suspected or confirmed cases in an area that is separate from other patients. Place patients in adequately ventilated single rooms if possible. When single rooms are not available, place all cases together in the same room and ensure there is at least 3 feet (1 meter) between patients.[\[295\]](#)
- Implement standard precautions at all times:[\[295\]](#)
  - Practice hand and respiratory hygiene
  - Give patients a medical mask to wear
  - Wear appropriate personal protective equipment
  - Practice safe waste management and environmental cleaning.
- Implement additional contact and droplet precautions before entering a room where cases are admitted:[\[295\]](#)
  - Wear a medical mask, gloves, an appropriate gown, and eye/facial protection (e.g., goggles or a face shield)
  - Use single-use or disposable equipment.
- Implement airborne precautions when performing aerosol-generating procedures, including placing patients in a negative pressure room.[\[295\]](#)
  - Some countries and organizations recommend airborne precautions for any situation involving the care of a COVID-19 patient.
- All specimens collected for laboratory investigations should be regarded as potentially infectious.[\[295\]](#)
- Appropriate personal protective equipment gives healthcare workers a high level of protection against COVID-19. A cross-sectional study of 420 healthcare workers deployed to Wuhan with appropriate personal protective equipment tested negative for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on molecular and serologic testing when they returned home, despite all participants having direct contact with COVID-19 patients and performing at least one aerosol-generating procedure.[\[296\]](#) Standard surgical masks are as effective as respirator masks for preventing infection of healthcare workers in outbreaks of viral respiratory illnesses such as influenza, but it is unknown whether this applies to COVID-19.[\[297\]](#)
- Detailed infection prevention and control guidance is available:
  - [\[WHO: infection prevention and control during health care when coronavirus disease \(COVID-19\) is suspected or confirmed\]](#)
  - [\[CDC: interim infection prevention and control recommendations for healthcare personnel during the coronavirus disease 2019 \(COVID-19\) pandemic\]](#)
  - [\[BMJ: covid-19 – PPE guidance\]](#)

## Telehealth for primary care physicians

- It is important that primary care physicians avoid in-person assessment of patients with suspected COVID-19 in primary care when possible to avoid infection.[\[298\]](#) Most patients can be managed remotely by telephone or video consultations. Algorithms for dealing with these patients are available:
  - [\[BMJ: covid-19 in primary care \(UK\)\]](#)
  - [\[BMJ: covid-19 – a remote assessment in primary care\]](#)

## General prevention measures for the general public

- People should be advised to:[\[299\]](#) [\[300\]](#)
  - Wash hands often with soap and water for at least 20 seconds or an alcohol-based hand sanitizer (that contains at least 60% alcohol), especially after being in a public place, blowing their nose, or coughing/sneezing. Avoid touching the eyes, nose, and mouth with unwashed hands
  - Avoid close contact with people (i.e., maintain a distance of at least 3 feet [1 meter]) including shaking hands, particularly those who are sick, have a fever, or are coughing or sneezing. Avoid going to crowded places. It is important to note that recommended distances differ between countries (for example, 6 feet [2 meters] is recommended in the US and UK) and you should consult local guidance. However, there is no evidence to support a distance of 6 feet (2 meters)[\[301\]](#)
  - Practice respiratory hygiene (i.e., cover mouth and nose when coughing or sneezing, discard tissue immediately in a closed bin, and wash hands)
  - Seek medical care early if they have a fever, cough, and difficulty breathing, and share their previous travel and contact history (travelers or suspected/confirmed cases) with their healthcare provider
  - Stay at home and self-isolate if they are sick, even with mild symptoms, until they recover (except to get medical care)
  - Clean and disinfect frequently touched surfaces daily (e.g., light switches, door knobs, countertops, handles, phones).
- [\[BMJ Learning: Covid-19 – handwashing technique and PPE videos\]](#)
- [\[WHO: coronavirus disease \(COVID-19\) advice for the public\]](#)
- [\[Centre for Evidence-Based Medicine: what is the evidence to support the 2-metre social distancing rule to reduce COVID-19 transmission?\]](#)

#### Face masks for the general public

- Recommendations on the use of face masks in community settings vary between countries.[\[302\]](#) It is mandatory to wear a mask in public in certain countries or in certain situations, and masks may be worn in some countries according to local cultural habits. Consult local guidance for more information.
- There is no high-quality or direct scientific evidence to support the widespread use of masks by healthy people in the community setting, and there are risks and benefits that must be considered.[\[77\]](#) [\[303\]](#) Evidence for mask effectiveness for respiratory tract infection prevention is stronger in healthcare settings compared with community settings; direct evidence on comparative effectiveness in SARS-CoV-2 infection is lacking.[\[304\]](#)
- The World Health Organization (WHO) recommends that people with symptoms of COVID-19 should wear a medical mask, self-isolate, and seek medical advice as soon as possible. The WHO also now encourages the general public to wear medical or cloth masks in specific situations and settings (e.g., areas with known or suspected widespread transmission and limited or no capacity to implement other containment measures such as social distancing, contact tracing, and testing; settings where social distancing cannot be achieved, particularly in vulnerable populations). This recommendation is based on observational evidence only.[\[77\]](#) The WHO does not recommend masks for the prevention of COVID-19 in the community setting in children under 5 years of age.[\[305\]](#)
- The Centers for Disease Control and Prevention (CDC) recommends that homemade cloth face coverings can be worn in public settings where social distancing measures are difficult to maintain (e.g., pharmacies, grocery stores), especially in areas where there is significant community transmission.[\[306\]](#)
- Use of a mask alone is insufficient to provide adequate protection, and they should be used in conjunction with other infection prevention and control measures such as frequent hand hygiene and social distancing. It is important to wash your hands with soap and water (or an alcohol-based

sanitizer) prior to putting on a face mask, and to remove it correctly. Used masks should be disposed of properly.[77]

- Potential harms and disadvantages of wearing masks include: potential increased risk of self-contamination due to manipulation of face mask and touching face/eyes, or when nonmedical masks are not changed when wet or soiled; headache and/or breathing difficulties; facial skin lesions, irritant dermatitis, or worsening acne; discomfort; difficulty communicating; social and psychological acceptance; false sense of security; poor compliance; waste management issues; and difficulties for patients with chronic respiratory conditions or breathing problems.[77] Masks may also create a humid habitat where the virus can remain active and this may increase viral load in the respiratory tract; deeper breathing caused by wearing a mask may push the virus deeper into the lungs.[307]
- In a study comparing the use of cloth masks to surgical masks in healthcare workers, the rates of all infection outcomes were highest in the cloth mask arm, with the rate of influenza-like illness statistically significantly higher in this group. Moisture retention, reuse of cloth masks, and poor filtration may result in increased risk of infection.[308] The filtration, fit, effectiveness, and performance of cloth masks are inferior to medical masks and respirators. Protection may be improved by selecting appropriate material, increasing the number of mask layers, and using masks with a design that provides filtration and fit.[309]
- [\[BMJ: facemasks for the prevention of infection in healthcare and community settings\]](#)
- [\[BMJ: analysis – face masks for the public during the covid-19 crisis\]](#)

#### Alcohol-based hand sanitizers

- The CDC has issued a warning about alcohol-based sanitizers containing methanol (which may be labeled as containing ethanol). Methanol poisoning should be considered in patients who present with relevant signs and symptoms (e.g., headache, impaired vision, nausea/vomiting, abdominal pain, loss of coordination, decreased level of consciousness) who report ingestion of hand sanitizer or frequent repeated topical use. Cases of permanent blindness and death have been reported.[310]
- Frequent use of hand sanitizers may result in antimicrobial resistance. Accidental ingestion, especially by children, has been reported.[311]

#### Screening and quarantine

- People traveling from areas with a high risk of infection may be screened using questionnaires about their travel, contact with ill persons, symptoms of infection, and/or measurement of their temperature. Combined screening of airline passengers on exit from an affected area and on arrival elsewhere has been relatively ineffective when used for other infections such as Ebola virus infection, and has been modeled to miss up to 50% of cases of COVID-19, particularly those with no symptoms during the incubation period.[312] Symptom-based screening processes have been reported to be ineffective in detecting SARS-CoV-2 infection in a small number of patients who were later found to have evidence of SARS-CoV-2 in a throat swab.[313]
- Enforced quarantine is being used to isolate easily identifiable cohorts of people at potential risk of recent exposure (e.g., groups evacuated by aeroplane from affected areas, people returning to their home countries before border closures, or groups on cruise ships with infected people on board).[314] The psychosocial effects of enforced quarantine may have long-lasting repercussions.[315] [316] Despite limited evidence, a Cochrane review found quarantine to be important in reducing the number of people infected and deaths, especially when started earlier and when used in combination with other prevention and control measures.[317]
- Travelers who arrive in the UK are required to self-isolate for 14 days unless they have traveled from an exempt country. [\[Public Health England: coronavirus \(COVID-19\) – how to self-isolate when you travel to the UK\]](#)

#### Social distancing

- Many countries have implemented mandatory social distancing measures in order to reduce and delay transmission (e.g., city lockdowns, stay-at-home orders, curfews, nonessential business closures, bans on gatherings, school and university closures, travel restrictions and bans, remote working, quarantine of exposed people/travelers).

- Although the evidence for social distancing for COVID-19 is limited, it is emerging, and the best available evidence appears to support social distancing measures to reduce the transmission and delay spread. The timing and duration of these measures appears to be critical.[318] [319]
- Researchers in Singapore found that social distancing measures (isolation of infected individuals and family quarantine, school closures, and workplace distancing) significantly decreased the number of infections in simulation models.[320]
- [Public Health England: staying alert and safe (social distancing)]

#### Shielding extremely vulnerable people

- Shielding is a measure used to protect vulnerable people (including children) who are at very high risk of severe illness from COVID-19 because they have an underlying health condition. Shielding involves minimizing all interactions between those who are extremely vulnerable and other people to protect them from coming into contact with the virus.
- Extremely vulnerable groups include:[321]
  - Solid organ transplant recipients
  - People with specific cancers
  - People with severe respiratory conditions (e.g., cystic fibrosis, severe asthma, or severe COPD)
  - People with rare diseases that significantly increase the risk of infections (e.g., sickle cell anemia, severe combined immunodeficiency)
  - People on immunosuppression therapies sufficient to significantly increase the risk of infection
  - Women who are pregnant with significant heart disease (congenital or acquired)
  - Other people who have also been classed as clinically extremely vulnerable based on clinical judgment and an assessment of their needs.
- The UK government recommended shielding for certain groups of people until 31 July, and paused shielding from 1 August. Shielding recommendations may be necessary again if community transmission begins to rise significantly. The easing of shielding restrictions does not apply to extremely vulnerable people living in areas that are under local lockdown.[321] Consult current guidance for specific recommendations (recommendations may differ between countries).
  - [Public Health England: guidance on shielding and protecting people who are clinically extremely vulnerable from COVID-19]
- Shielding advice for children and young adults is available. Shielding of clinically extremely vulnerable children and young people is not currently recommended in the UK. Consult current guidance for specific recommendations (recommendations may differ between countries).
  - [Public Health England: guidance for young people on shielding and protecting people most likely to become unwell if they catch coronavirus]
  - [Royal College of Paediatrics and Child Health: COVID-19 – 'shielding' guidance for children and young people]

#### Vaccines

- Several vaccine candidates are currently approved for human testing through clinical trials, including mRNA and DNA platform vaccines, adenovirus vector vaccines, spike glycoprotein nanoparticle vaccines, and inactivated virus vaccines.[322]
- Russia became the first country in the world to approve a vaccine in early August.[323] However, only phase 1/2 results (76 participants) have been published so far.[324]
- Previous trials of coronavirus vaccines identified cellular immunopathology and antibody-dependent enhancement (ADE) as potential safety issues, so there are concerns over ADE of SARS-CoV-2 due to prior exposure to other coronaviruses (such as those that cause the common cold).[325] [326]
- Results from preliminary animal and human studies are now available, but scientists urge caution over the results.[327]

- Ad5-nCoV: a recombinant adenovirus type-5 (Ad5) vectored vaccine expressing the SARS-CoV-2 spike glycoprotein. Results from a single-center, open-label, nonrandomized, dose-escalation phase 1 trial in China report that the vaccine was immunogenic, inducing humoral responses (peaking 28 days after vaccination) and T-cell responses (peaking 14 days after vaccination) in most participants. Participants were healthy and had no underlying diseases. At least one adverse reaction was reported within the first 7 days after vaccination in 83% (low- and medium-dose groups) and 75% (high-dose group) of participants. The most common adverse reactions reported included injection-site reactions, fever, fatigue, headache, and muscle pain. No serious adverse events were noted within 28 days of vaccination.[328] A phase 2 randomized, double-blind, placebo-controlled trial in around 500 healthy adults (50% male, mean age 39 years) found that the vaccine induced a significant immune response in the majority of patients after a single dose of either the  $1 \times 10^{11}$  or the  $5 \times 10^{10}$  viral particle dose at day 28. Adverse reactions were significantly higher in the Ad5-nCoV group compared with placebo, and were reported in 72% of participants in the  $1 \times 10^{11}$  viral particle dose group and 74% of participants in the  $5 \times 10^{10}$  viral particle dose group.[329]
- AZD1222 (formerly known as ChAdOx1 nCoV-19): an adenovirus vector vaccine that carries the SARS-CoV-2 spike protein. Preliminary results (not peer reviewed) from animal studies found that a single dose induced a humoral and cellular response in mice and rhesus macaques. However, while viral loads in bronchoalveolar lavage fluid and lung tissues of vaccinated animals were significantly reduced compared with unvaccinated animals, reduction in viral shedding from the nose was not observed.[330] A phase 1/2, single-blind, randomized controlled trial in young healthy volunteers that used the meningococcal conjugate vaccine as a control found that AZD1222 was immunogenic. Local and systemic reactions were more common in the AZD1222 group and no serious adverse events were reported in the 28 days following vaccination.[331] The UK-based phase 3 trial was halted in early September after a vaccine participant experienced an unexplained illness.[332] News reports suggested that the participant developed transverse myelitis, a serious adverse event reported with almost all vaccines. The trial has now resumed in the UK following confirmation by the UK Medicines and Healthcare products Regulatory Agency (MHRA) that it was safe to do so. The company has not disclosed the nature of the adverse event.[333]
- Inactivated SARS-CoV-2 virus (Sinovac®): contains a more traditional chemically inactivated version of the virus. The vaccine was found to induce immunity in mice, rats, and nonhuman primates. When challenged with the virus, monkeys who were vaccinated with the highest dose of the vaccine did not develop infection, and no virus was recovered from the throat, lung, or rectum.[334] In an interim analysis of two ongoing randomized controlled trials in healthy adults ages 18 to 59 years, a phase 1 trial of 96 participants and a phase 2 trial of 224 participants, the vaccine induced a neutralizing antibody response by 14 days. The studies compared the vaccine with an alum adjuvant. The incidence of adverse effects across all participants within 7 days of injection was 15%, most commonly injection-site reactions and fever. Although the vaccine elicited an antibody response, it is unknown whether this could protect individuals against COVID-19.[335]
- mRNA-1273: a novel vaccine that uses mRNA technology not previously approved for use in humans. The mRNA encodes for a full-length prefusion stabilized spike protein of SARS-CoV-2 and is encapsulated in a lipid nanoparticle. Results from a phase 1 trial indicated that all 45 healthy adults (ages 18-55 years) who were given 2 injections (25, 100, or 250 micrograms) of the vaccine 28 days apart seroconverted by day 15 after the first dose. All dose groups had antibody levels in the top quartile for convalescent serum after the second vaccination. Systemic adverse events occurred more frequently after the second vaccination and occurred in 54% of participants in the 25-microgram group, and 100% of participants in the 100-microgram and 250-microgram groups. Of the cohort of 14 patients who received the highest dose (250 micrograms), 21% of participants experienced one or more severe adverse events following the second dose. One participant in the 25-microgram group was withdrawn due to transient urticaria related to the first vaccination. The study did not include people with underlying conditions.[336] mRNA-1273 has been granted fast-track designation by the Food and Drug Administration (FDA), and phase 3 trials have started.
- NVX-CoV2373: a recombinant SARS-CoV-2 nanoparticle vaccine composed of trimeric, full-length, SARS-CoV-2 spike glycoproteins and Matrix-M1® adjuvant (an adjuvant based on saponin extracted from the *Quillaja saponaria* Molina tree). A phase 1/2 randomized, placebo controlled trial in 131 healthy adults ages 18 to 59 years in Australia found that NVX-CoV2373 elicited immune responses that exceeded levels in COVID-19 convalescent serum at 35 days.[337]
- BNT162b1: a lipid nanoparticle-formulated, nucleoside-modified, mRNA vaccine that encodes spike glycoprotein RBD. Preliminary (not peer reviewed) phase 1/2 study results in healthy adults ages 18 to 55 years have been published. RBD-binding immunoglobulin G antibodies and SARS-

CoV-2 neutralizing antibodies were detected in all subjects at 28 days after two doses. Adverse reactions were dose-dependent and reported in 50% of subjects who received the 10 microgram or 30 microgram dose, and by 58% of subjects who received the 100 microgram dose.[338] BNT162b1 and BNT162b2 (its related vaccine candidate) have been granted fast-track designation by the FDA. A global phase 2/3 trial of BNT162b2 has started.

- Results from other vaccine candidates are becoming available; however, a detailed discussion of all vaccine candidates is beyond the scope of this topic.
- The FDA has issued guidance to vaccine developers that in order for it to approve a vaccine candidate the primary efficacy end-point point estimate for a placebo-controlled efficacy trial should be at least 50%, and the statistical success criterion should be that the lower bound of the appropriately alpha-adjusted confidence interval around the primary efficacy end-point point estimate is >30%.[339]

#### Pre-exposure or postexposure prophylaxis

- There are no drugs recommended for pre-exposure prophylaxis or postexposure prophylaxis, except in the context of a clinical trial.[3] See the Emerging section for more information.

#### Immunity passports

- Some governments are discussing or implementing certifications for people who have contracted and recovered from COVID-19 based on antibody tests (sometimes called "immunity passports"). Possession of a passport would allow people to have a greater range of privileges (e.g., work, education, travel). However, the WHO does not support these certifications as there is currently no evidence that people who have recovered from infection and have antibodies are protected from reinfection.[340] Other potential issues include lack of public support for these measures, potential for discrimination of groups of people, testing errors (including cross-reactivity with other human coronaviruses), access to testing, fraud, legal and ethical objections, and people getting infected intentionally in order to obtain a certification.[341]

#### Smoking cessation

- Past or current smokers have nearly double the risk for severe disease, and smoking cessation should be encouraged.[342] The WHO recommends that tobacco users stop using tobacco given the well-established harms associated with tobacco use and second-hand smoke exposure.[235] Public Health England also recommends stopping smoking. [Public Health England: COVID-19 – advice for smokers and vapers]

## Screening

### Management of contacts

A contact is a person who has experienced any one of the following exposures during the 2 days before and the 14 days after the onset of symptoms of a probable or confirmed case:[478]

- Face-to-face contact with a probable or confirmed case within 3 feet (1 meter) and for more than 15 minutes
- Direct physical contact with a probable or confirmed case
- Direct care for a patient with probable or confirmed COVID-19 without using recommended personal protective equipment
- Other situations as indicated by local risk assessments.

Contacts should remain in quarantine at home and monitor their health for 14 days from the last day of possible contact with the infected person. Local surveillance guidelines should be followed.

## Screening of travelers

Exit and entry screening may be recommended in countries where borders are still open, particularly when repatriating nationals from affected areas. Travelers returning from affected areas should self-monitor for symptoms for 14 days and follow local protocols of the receiving country. Some countries may require travelers to enter mandatory quarantine in a designated location (e.g., a hotel). Travelers who develop symptoms are advised to contact their local healthcare provider, preferably by phone.<sup>[479]</sup> One study of 566 repatriated Japanese nationals from Wuhan City found that symptom-based screening performed poorly and missed presymptomatic and asymptomatic cases. This highlights the need for testing and follow-up.<sup>[480]</sup>

## Drive-through screening centers

Drive-through screening centers have been set up in some countries for safer and more efficient screening. The testee does not leave their car throughout the entire process, which includes registration and questionnaire, exam, specimen collection, and instructions on what to do after. This method has the advantage of increased testing capacity and prevention of cross-infection between testees in the waiting space.<sup>[481]</sup>

## Temperature screening

There is little scientific evidence to support temperature screening with thermal cameras or temperature screening products as a reliable method for the detection of COVID-19 or any other febrile illness, especially if used as the main method of testing.<sup>[482]</sup>

## Case history

### Case history #1

A 61-year-old man presents to the hospital with fever, dry cough, and difficulty breathing. He also reports feeling very tired and unwell. He has a history of hypertension, which is controlled with enalapril. On exam, his pulse is 120 bpm, his temperature is 101.6°F (38.7°C), and his oxygen saturation is 88%. He appears acutely ill. He is admitted to hospital in an isolation room and is started on oxygen, intravenous fluids, and empiric antibiotics. Chest x-ray shows bilateral lung infiltrates, and computed tomography of the chest reveals multiple bilateral lobular and subsegmental areas of ground-glass opacity. A nasopharyngeal swab is sent for real-time reverse transcriptase polymerase chain reaction testing, and the result comes back positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) the next day. The patient develops respiratory distress 7 days after admission and is transferred to the intensive care unit and started on mechanical ventilation.

### Case history #2

A 26-year-old woman calls her doctor complaining of a sore throat and a persistent dry cough. She denies having a fever, and has not traveled in the last 14 days or knowingly been in contact with a confirmed case of COVID-19. She is advised to stay at home and self-isolate and to call her doctor if her symptoms get worse.

### Other presentations

See the Diagnosis section for more information on other presentations.

## Step-by-step diagnostic approach

Early recognition and rapid diagnosis are essential to prevent transmission and provide supportive care in a timely manner. Have a high index of clinical suspicion for COVID-19 in all patients who present with fever and/or acute respiratory illness; however, be aware that some patients may not present with signs or symptoms of a febrile respiratory illness.

COVID-19 care pathways should be established at local, regional, and national levels for people with suspected or confirmed COVID-19. Screen patients at the first point of contact within the health system based on case definitions and an assessment of symptoms, and enter suspected or confirmed cases into the pathway.<sup>[2]</sup> Immediately isolate all suspected and confirmed cases and implement local infection prevention and control procedures. Triage patients with a standardized triage tool and evaluate the patient to assess the severity of disease. COVID-19 is a notifiable disease. Suspected cases should remain in the pathway until proven negative.

Best Practice has published a separate topic on the management of coexisting conditions in the context of COVID-19. [\[BMJ Best Practice: Management of coexisting conditions in the context of COVID-19\]](#)

## Key recommendations

- Isolate all suspected or confirmed cases immediately. Triage patients with a standardized triage tool and evaluate the severity of disease. Follow local infection prevention and control guidelines.[2]
- Have a high index of clinical suspicion in all patients who present with fever and/or acute respiratory illness. People with a history of residence/work/travel in a location with a high risk of transmission or community transmission and contacts of probable and confirmed cases are at higher risk of infection.[153]
- Suspect the diagnosis in patients with a new continuous cough, fever, or altered sense of taste or smell.[343] Patients may also present with symptoms including dyspnea, fatigue, myalgia/arthralgia, sore throat, headache, nasal congestion or rhinorrhea, sputum production, chest tightness, or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea).[344]
- Order a real-time reverse transcription polymerase chain reaction (RT-PCR) to confirm the diagnosis. Upper and lower respiratory specimens are preferred. Serologic testing may be useful in some settings.[345]
- Be on high alert for children and adolescents with acute gastrointestinal symptoms and signs of cardiac inflammation. Evidence so far suggests a milder or asymptomatic course of disease in children.[346] However, a rare multisystem inflammatory condition with some features similar to those of Kawasaki disease and toxic shock syndrome has been temporally associated with COVID-19 in children and adolescents.[347]
- Order the following laboratory investigations in hospitalized patients: complete blood count, comprehensive metabolic panel, arterial blood gas, blood glucose level, coagulation screen, inflammatory markers, cardiac biomarkers, serum creatine kinase, and blood and sputum cultures for other pathogens. Pulse oximetry may reveal low oxygen saturation.
- Prioritize a chest x-ray in patients who are seriously ill with suspected pneumonia. Consider a computed tomography scan of the chest if chest x-ray is uncertain or normal.[348] Consult local guidelines.
- Report all suspected or confirmed cases to your local health authorities. COVID-19 is a notifiable disease.
- For full details and guidance see information below.

## History

Take a detailed history to ascertain the level of risk for COVID-19 and assess the possibility of other causes, including a travel history and an assessment of risk factors.

Diagnosis should be suspected in:[153]

- People residing or working in an area with a high risk of transmission (e.g., closed residential settings, humanitarian setting), people residing in or traveling to an area with community transmission, and people working in a health setting (including within health facilities and households) at any time within the 14 days prior to symptom onset
- People who have had contact with a probable or confirmed case. A contact is a person who has experienced any one of the following exposures during the 2 days before and the 14 days after the onset of symptoms of a probable or confirmed case:
  - Face-to-face contact with a probable or confirmed case within 3 feet (1 meter) and for at least 15 minutes

- Direct physical contact with a probable or confirmed case
- Direct care for a patient with probable or confirmed COVID-19 without using recommended personal protective equipment
- Other situations as indicated by local risk assessments.

## Clinical presentation in adults

Approximately 15% of patients present with the symptom triad of fever, cough, and dyspnea, and 90% present with more than one symptom.[32] Some patients may be minimally symptomatic or asymptomatic, while others may present with severe pneumonia or complications such as acute respiratory syndrome, septic shock, acute myocardial infarction, venous thromboembolism, or multi-organ failure.

The most common symptoms are:

- Fever
- Cough
- Dyspnea
- Altered sense of taste/smell.

Less common symptoms include:

- Myalgia or arthralgia
- Fatigue
- Sputum production
- Chest tightness
- Gastrointestinal symptoms
- Sore throat
- Headache
- Dizziness
- Neurologic symptoms
- Ocular symptoms
- Cutaneous symptoms
- Rhinorrhea/nasal congestion
- Chest pain
- Hemoptysis.

Signs and symptoms of febrile respiratory illness may not possess the necessary sensitivity for early diagnostic suspicion.[349] A Cochrane review found that at least half of patients had a cough, sore throat, fever, myalgia/arthralgia, fatigue, or headache. The presence of fever, myalgia/arthralgia, fatigue, and headache substantially increased the likelihood of COVID-19 when present. Cough and sore throat were common in people without COVID-19, so these symptoms alone were less helpful for diagnosis. No single symptom or sign included in the review could accurately diagnose COVID-19 and the authors concluded that neither the absence or presence of signs or symptoms are accurate enough to rule in or rule out disease.[344]

The clinical presentation has varied slightly across geographic locations. Initial impressions from the US note that the clinical presentation may be broader than that observed in China and Italy, with chest pain, headaches, altered mental status, and gastrointestinal symptoms all observed on initial presentation. Severe hepatic and renal dysfunction that spares the lungs has also been observed.[350] Data from the first hospitalized patients in New York found that while the most common presenting symptoms were

fever, cough, dyspnea, and myalgia, gastrointestinal symptoms appeared to be more common than in China.[351]

In terms of severity:[4]

- 80% of adults present with mild to moderate illness
- 14% of adults present with severe illness
- 5% of adults present with critical illness
- 1% of adults present with asymptomatic illness.

The most prevalent symptoms in patients with mild to moderate illness, according to one European study, are headache, loss of smell, nasal congestion, cough, asthenia, myalgia, rhinorrhea, gustatory dysfunction, and sore throat. Fever was reported less commonly. The mean duration of symptoms was 11.5 days. The presentation varied according to age, with younger patients generally having ear, nose, and throat complaints, and older patients generally having fever, fatigue, and loss of appetite.[352] More common symptoms in patients with severe disease include fever, dyspnea, and anorexia.[106]

Pregnant women

- The clinical characteristics in pregnant women are similar to those reported for nonpregnant adults.[353] The most common symptoms in pregnant women are fever and cough. However, pregnant women are less likely to report fever and myalgia compared with nonpregnant women of reproductive age.[354]
- It is important to note that symptoms such as fever, dyspnea, gastrointestinal symptoms, and fatigue may overlap with symptoms due to physiologic adaptations of pregnancy or adverse pregnancy events.[2]

Atypical presentations

- Atypical presentations may occur, especially in older patients and patients who are immunocompromised (e.g., falls, delirium/confusion, functional decline, reduced mobility, syncope, persistent hiccups, absence of fever). Older patients and those with comorbidities may present with mild symptoms, but have a high risk of deterioration.[2]
- There have been case reports of parotitis (possibly related to intraparotid lymphadenitis), oral vesiculobullous lesions, retinal lesions, and androgenetic alopecia in patients with COVID-19; however, it is unknown whether these findings are associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection as yet.[355] [356] [357] [358]

Coinfections

- The pooled prevalence of coinfection with viruses and atypical bacteria in SARS-CoV-2-positive patients was 11.6% (16.8% in studies that tested 100% of patients for copathogens).[359]
- Bacterial coinfections have been reported in 7% of hospitalized patients, and 14% of patients in intensive care units. The most common bacteria were *Mycoplasma pneumoniae*, *Pseudomonas aeruginosa*, *Haemophilus influenzae*, and *Klebsiella pneumoniae*. Coinfections with fungal pathogens and viruses (e.g., respiratory syncytial virus, influenza A) were less commonly reported.[360]
- Coinfections are more common in critically ill patients.[361]
- Coinfections may be associated with protracted respiratory symptoms, prolonged intensive care stay, morbidity, and mortality if not detected and treated early.[362]

- Patients with influenza coinfection showed similar clinical characteristics to patients with COVID-19 only.[363] [364]

## Clinical presentation in children

Signs and symptoms may be similar to other common viral respiratory infections and other childhood illnesses, so a high index of suspicion for COVID-19 is required in children.

In terms of severity:[365]

- 33% of children present with mild illness
- 51% of children present with moderate illness
- 7% of children present with severe illness
- 5% of children present with critical illness
- 20% of children present with asymptomatic illness.

Evidence so far suggests a milder, or asymptomatic, course of disease in about 95% of children, but with possible evidence of radiologic lung changes in both categories. Symptoms commonly reported include fever, cough, sore throat, nasal congestion, and rhinorrhea. Fever, cough, and dyspnea are less common in children compared with adults. Children may present with gastrointestinal symptoms more commonly than adults, particularly newborns and infants, and these may be the only symptom.[346] Febrile seizures have been reported rarely.[9] The clinical manifestations in children under 5 years of age appear to be milder compared with those of influenza A infection.[366]

Severe disease has been reported rarely in children.[346] [367] In a cross-sectional study of 48 critically ill infants and children in the US, the clinical course and hospital outcomes were better compared with adults. Similar to adults, 80% of critically ill children had preexisting comorbidities, most commonly immune suppression/cancer, cardiac disease, obesity, and diabetes.[368] [369] It is worth noting that critical disease has been reported more frequently in children under 1 year of age compared with children older than 1 year of age, and vomiting is more common in this age group.[365] There is increasing concern that a related inflammatory syndrome is emerging in children with severe disease. See the Complications section for more information.

Cases of COVID-19 have been reported in neonates. Dyspnea is the most common sign in neonates. Although illness is usually mild, severe illness, including cases of late-onset neonatal sepsis and encephalitis, has been reported. Severe illness is slightly more common in neonates compared with older children. Infants may present with irritability, crying, feeding difficulties, silent hypoxia, and neurologic symptoms.[346] [370] [371] [372]

Coinfections may be more common in children.[373] Coinfection was documented in 6% of children in US and Italian studies, with the most common pathogens being respiratory syncytial virus, rhinoviruses, Epstein-Barr virus, enteroviruses, influenza A, non-SARS coronaviruses, and *Streptococcus pneumoniae*. [9] [180]

## Physical exam

Perform a physical exam. Avoid use of a stethoscope if possible due to risk of viral contamination. Patients may be febrile (with or without chills/rigors) and have obvious cough and/or difficulty breathing. Auscultation of the chest may reveal inspiratory crackles, rales, and/or bronchial breathing in patients with pneumonia or respiratory distress. Patients with respiratory distress may have tachycardia, tachypnea,

or cyanosis accompanying hypoxia. Bradycardia has been noted in a small cohort of patients with mild to moderate disease.[374]

## Pulse oximetry

Pulse oximetry may reveal low oxygen saturation ( $SpO_2 < 90\%$ ). Clinicians should be aware that patients with COVID-19 can develop "silent hypoxia": their oxygen saturations can drop to low levels and precipitate acute respiratory failure without the presence of obvious symptoms of respiratory distress. Only a small proportion of patients have other organ dysfunction, meaning that after the initial phase of acute deterioration, traditional methods of recognizing further deterioration (e.g., National Early Warning Score 2 [NEWS2] scores) may not help predict those patients who go on to develop respiratory failure.[375]

While NEWS2 is still recommended for use in patients with COVID-19, the UK Royal College of Physicians now advises that any increase in oxygen requirements in these patients should trigger an escalation call to a competent clinical decision maker, and prompt an initial increase in observations to at least hourly until a clinical review happens.[376]

## Initial laboratory investigations

Order the following laboratory investigations in all patients with severe illness:

- ABG
- CBC
- Comprehensive metabolic panel
- Blood glucose level
- Coagulation screen
- Inflammatory markers (e.g., serum C-reactive protein, erythrocyte sedimentation rate, interleukin-6, lactate dehydrogenase, procalcitonin, amyloid A, and ferritin)
- Cardiac biomarkers
- Serum creatine kinase and myoglobin.

The most common laboratory abnormalities are lymphopenia, leukocytosis, leukopenia, thrombocytopenia, hypoalbuminemia, elevated cardiac biomarkers, elevated inflammatory markers, elevated D-dimer, and abnormal liver and renal function.[351] [377] [378] [379] Laboratory abnormalities – in particular, lymphopenia, leukocyte abnormalities, and other markers of systemic inflammation – are less common in children.[346] [380] [381] Most patients (62%) with asymptomatic disease present with normal laboratory parameters. Of those with laboratory abnormalities, leukopenia, lymphopenia, elevated lactate dehydrogenase, and elevated C-reactive protein were the most common findings.[382]

Collect blood and sputum specimens for culture in patients with severe or critical disease to rule out other causes of lower respiratory tract infection and sepsis, especially patients with an atypical epidemiologic history. Specimens should be collected prior to starting empiric antimicrobials if possible.[2]

## Molecular testing

Molecular testing is required to confirm the diagnosis. Order a nucleic acid amplification test, such as real-time reverse-transcription polymerase chain reaction (RT-PCR), for SARS-CoV-2 in patients with suspected infection whenever possible (see the Criteria section).[345] Tests should be performed according to guidance issued by local health authorities and adhere to appropriate biosafety practices.

## Who to test

- Base decisions about who to test on clinical and epidemiologic factors.[345]
- In the UK, testing is recommended in:[343] [383]
  - People in the community with symptoms of new continuous cough, high temperature, or altered sense of smell/taste
  - People requiring hospital admission and who have clinical or radiologic evidence of pneumonia, or acute respiratory distress syndrome, or influenza-like illness, or altered sense of smell/taste in isolation or in combination with any other symptoms.
- In the US, testing is recommended in:[384]
  - People with symptoms, even if they are mild
  - People who are asymptomatic and have been in close contact for at least 15 minutes with a person with documented infection
  - People who are asymptomatic and have not been in close contact for at least 15 minutes with a person with documented infection only if required by a healthcare provider or public health official.
- Consult local health authorities for guidance as testing priorities depend on local recommendations and available resources.

## Specimens

- The optimal specimen for testing depends on the clinical presentation and the time since symptom onset. The World Health Organization (WHO) recommends the following.[345]
  - Upper respiratory specimens: recommended for early-stage infections, especially asymptomatic or mild cases. Nasopharyngeal swabs yield a more reliable result than oropharyngeal swabs; combined nasopharyngeal and oropharyngeal swabs further improve reliability.
  - Lower respiratory specimens: recommended for later-stage infections, or patients in whom there is a strong suspicion for infection and their upper respiratory tract specimen test was negative. Suitable specimens are sputum and/or endotracheal aspirate or bronchoalveolar lavage in patients with more severe respiratory disease. However, consider the high risk of aerosol transmission when collecting lower respiratory specimens – an induced sputum specimen is not recommended as it may increase the risk of aerosol transmission.
  - Other respiratory specimens: studies on combined oropharyngeal and nares/nasal swabs, mid-turbinate or lower nasal or nares swabs, or tongue swabs have been conducted; however, further assessment and validation is required. Oral fluid collection may be suitable in some circumstances (e.g., young children, older patients with dementia). There is emerging evidence that saliva may be a reliable specimen for diagnosis.[385] [386] [387] [388] However, the WHO does not currently recommend the use of saliva as the sole specimen type for routine clinical diagnostics.
  - Fecal specimens: consider when upper or lower respiratory specimens are negative and the clinical suspicion for infection remains (may be used from the second week after symptom onset).

- Recommended specimen types may differ between countries. For example, in the US, the Centers for Disease Control and Prevention (CDC) recommends the following upper respiratory specimens: nasopharyngeal or oropharyngeal swab; nasal mid-turbinate swab; anterior nares swab; or nasopharyngeal/nasal wash/aspirate. Recommended lower respiratory tract specimens include: sputum, bronchoalveolar lavage, tracheal aspirate, pleural fluid, and lung biopsy.[389]
- Collect specimens under appropriate infection prevention and control procedures.

#### Test result

- A positive RT-PCR result confirms SARS-CoV-2 infection. If the result is negative, and there is still a clinical suspicion of infection (e.g., an epidemiologic link, typical x-ray findings, absence of another etiology), resample the patient and repeat the test. A positive result confirms infection. If the second test is negative, consider serologic testing (see below).[345]
- Genomic sequencing is not routinely recommended, but may be useful to investigate the dynamics of an outbreak, including changes in the size of an epidemic over time, its spatiotemporal spread, and testing hypotheses about transmission routes.[345]

#### Testing for other infections

- Collect nasopharyngeal swabs for testing to rule out infection with other respiratory pathogens (e.g., influenza, atypical pathogens) when clinically indicated according to local guidance. Depending on local epidemiology and clinical symptoms, test for other potential causes including malaria, dengue fever, and typhoid fever as appropriate. It is important to note that coinfections can occur, and a positive test for a non-COVID-19 pathogen does not rule out COVID-19.[2] [390]

## Limitations of molecular testing

Interpret RT-PCR results with caution. RT-PCR detects viral RNA but it is not fully understood how that represents infectious virus, which ultimately could lead to restrictions for people who do not present an infection risk. Few studies have attempted to culture live SARS-CoV-2 virus from human samples. This is an issue because viral culture is regarded as a gold standard test against which any diagnostic index test for viruses must be measured and calibrated, to understand the predictive properties of that test.[391] Prospective routine testing of reference and viral culture specimens is necessary to establish the usefulness and reliability of RT-PCR to diagnose COVID-19, and its relation to patients factors such as date of onset of symptoms and copy threshold, in order to help predict infectivity.[392]

The pooled sensitivity of RT-PCR is 86%, and the pooled specificity is 96%. Accuracy depends on the prevalence of the disease in a given population; the lower the prevalence of disease, the lower the post-test probability.[393] Interpreting the test result also depends on the accuracy of the test, and the pretest probability (or estimated risk of disease) before testing.[394]

For example, if a test with a specificity of 99% is used to test a high-risk symptomatic population where the likelihood of infection is 50%, the positive predictive value is 99%. This means that for every 100 people with a positive test result, 99 people will have SARS-CoV-2 infection but 1 person without infection will have a false-positive result. Conversely, in a low-risk asymptomatic population where the likelihood of infection is low (e.g., 0.05%), the positive predictive value is around 4.3%. This means that for every 100 people with a positive test result, 4 to 5 people will have SARS-CoV-2 infection, but 95 to 96 people without infection will have a false-positive result.[395]

There is a lack of data on the rate of false-positive tests. False-positive results are more likely when the prevalence of SARS-CoV-2 is moderate to low.[396] False-positive results can be caused by a laboratory error or a cross-reaction with antibodies formed by current and past exposure to seasonal human coronavirus infections (e.g., common cold).[397]

False-negative rates of between 2% and 29% have been reported.[394] The probability of a false-negative result in an infected person decreases from 100% on day 1 of infection to 67% on day 4. The median false-negative rate drops to 38% on the day of symptom onset, decreases to 20% on day 8, and then starts to increase again from day 9.[398]

## Serologic testing

Serology cannot be used as a standalone diagnostic test for acute SARS-CoV-2 infections; however, it may be useful in various settings (e.g, negative molecular testing, diagnosing patients with late presentation or prolonged symptoms, serosurveillance studies).[345] [399]

[BMJ practice pointer: testing for SARS-CoV-2 antibodies]

The WHO recommends collecting a paired serum sample, one specimen in the acute phase and one in the convalescent phase 2 to 4 weeks later, in patients where infection is strongly suspected and the RT-PCR result is negative.[345]

- Seroconversion or a rise in antibody titers in paired sera help to confirm whether the infection is recent and/or acute. If the initial sample tests positive, this could be due to a past infection that is not related to the current illness.
- Seroconversion may be faster and more robust in patients with severe disease compared with those with mild disease or asymptomatic infection.

The CDC recommends serologic testing as a method to support the diagnosis of acute infection in patients who present late (i.e., 9 to 14 days after symptom onset) in addition to other viral detection methods (e.g., RT-PCR, antigen detection tests), or patients who present with late complications (e.g., pediatric inflammatory multisystem syndrome in children).[400]

- Assays with Food and Drug Administration emergency-use authorization are preferred. There is no advantage of assays whether they test for immunoglobulin G (IgG), IgM and IgG, or total antibody.
- The test's positive predictive value should be optimized by choosing tests with high specificity (e.g., >99.5%) and testing people or populations with a high pretest probability of having antibodies, or using an orthogonal testing algorithm. Results should be interpreted in the context of the expected predictive values (positive and negative).

The Infectious Diseases Society of America recommends serologic testing in the following circumstances:[401]

- Evaluation of patients with a high clinical suspicion for infection when molecular diagnostic testing is negative and at least 2 weeks have passed since symptom onset
- Evaluation of pediatric inflammatory multisystem syndrome in children
- Serosurveillance studies.

Antibody responses to SARS-CoV-2 typically occur during the first 1 to 3 weeks of illness, with the seroconversion time of IgG antibodies often being earlier than that of IgM antibodies.[402] [403]

A Cochrane review found that antibody tests for IgG/IgM only detected 30% of people with COVID-19 when the test was performed 1 week after the onset of symptoms, but accuracy increased in week 2 with 70% detected and week 3 with over 90% detected. Data beyond 3 weeks were limited. Tests gave false-positive results in 2% of patients without COVID-19. The review found that the sensitivity of antibody tests is too low in the first week since symptom onset to have a primary role in the diagnosis of COVID-19, but tests are likely to have a useful role in detecting previous infection if used 15 or more days after symptom onset (although there were very little data beyond 35 days).[404]

## Limitations of serologic testing

Understanding of the antibody response to SARS-CoV-2 is still emerging; therefore, antibody detection tests must be used with caution, and not used to determine acute infections.[345]

- Results do not indicate the presence or absence of current or previous infection with certainty as IgM and IgG antibodies may take 1 to 3 weeks to develop after infection.[400] A reliable diagnosis is often only possible in the recovery phase when opportunities for management or interruption of transmission have passed.[345]
- The duration of the persistence of antibodies produced in response to SARS-CoV-2 is still under investigation.[345] Some people may not develop detectable antibodies after infection, and in those who do, antibody levels may wane over time to undetectable levels.[400] The presence of antibodies that bind to SARS-CoV-2 does not guarantee that they are neutralizing antibodies, or that they offer protective immunity.[345]
- Some tests may exhibit cross-reactivity with other coronaviruses, such as those that cause the common cold, which can result in false-positive results.[400]
- Tests should not be used to determine the immune status of an individual, or to make decisions about grouping people residing in or being admitted to congregate settings (e.g., schools, dormitories, correctional facilities) or people returning to their workplace.[400]

## Rapid diagnostic tests

### Antibody detection

- While rapid antibody detection kits have been approved for the qualitative detection of SARS-CoV-2 IgG/IgM antibodies in serum, plasma, or whole blood, the WHO does not recommend the use of these tests outside of research settings as they have not been validated as yet.[405]
- Evidence is particularly weak for point-of-care serologic tests. A meta-analysis found that the overall sensitivity of chemiluminescent immunoassays (CLIAs) for IgG or IgM was approximately 98%, and the sensitivity of enzyme-linked immunosorbent assays (ELISAs) was 84%; however, lateral flow immunoassays (LFIAs), which have been developed as point-of-care tests, had the lowest sensitivity at 66%. Test sensitivity was highest 3 or more weeks after onset of symptoms. Available evidence does not support the use of existing point-of-care serologic tests.[406]

### Antigen detection

- Antigen testing relies on direct detection of SARS-CoV-2 viral proteins in nasal swabs and other respiratory specimens using a lateral flow immunoassay. Results are usually available in less than 30 minutes. While antigen tests are substantially less sensitive than RT-PCR, they offer the possibility of rapid, inexpensive, and early detection of the most infectious cases in

appropriate settings. If used, testing should occur within the first 5 to 7 days following the onset of symptoms.[407]

- The WHO recommends antigen testing only in certain scenarios where RT-PCR is unavailable or where prolonged turnaround times preclude clinical utility, provided that the test meets the minimum performance requirements of  $\geq 80\%$  sensitivity and  $\geq 97\%$  specificity compared with a RT-PCR reference assay.[407]

## Chest imaging

All imaging procedures should be performed according to local infection prevention and control procedures to prevent transmission. Chest imaging is considered safe in pregnant women.[408]

Order a chest x-ray in all patients with suspected pneumonia. Unilateral lung infiltrates are found in 25% of patients, and bilateral lung infiltrates are found in 75% of patients.[31] [32] [409] Although chest x-ray appears to have a lower sensitivity compared with chest CT, it has the advantages of being less resource-intensive, associated with lower radiation doses, easier to repeat sequentially, and portable.[410]

Consider ordering a CT scan of the chest. CT imaging is the primary imaging modality in some countries, such as China. It may be helpful in making the diagnosis, guiding individual patient management decisions, aiding the diagnosis of complications, or giving clues to an alternative diagnosis. However, it is not diagnostic for COVID-19 and local guidance should be consulted on whether to perform a CT scan.

The British Society of Thoracic Imaging (BSTI) recommends CT imaging in patients with clinically suspected COVID-19 who are seriously ill if chest x-ray is uncertain or normal. Without the suspicion of COVID-19, the radiology is nonspecific and could represent many other disease processes. The BSTI in collaboration with NHS England have produced a radiology decision support tool to help clinicians decide whether or not chest imaging should be ordered.[348]

[BSTI: radiology decision tool for suspected COVID-19]

Some institutions in the UK recommend a more pragmatic approach for patients with high clinical suspicion of COVID-19, with chest CT recommended only after two indeterminate or normal chest x-rays in combination with a negative RT-PCR test.[411]

The American College of Radiology recommends reserving CT for hospitalized, symptomatic patients with specific clinical indications for CT, and emphasizes that a normal chest CT does not mean that a patient does not have COVID-19 and that an abnormal chest CT is not specific for COVID-19 diagnosis.[412]

Abnormal chest CT findings have been reported in up to 97% of COVID-19 patients in one meta-analysis of 50,466 hospitalized patients.[413] Evidence of pneumonia on CT may precede a positive RT-PCR result for SARS-CoV-2 in some patients.[414] CT imaging abnormalities may be present in asymptomatic patients. The pooled estimate of the rate of positive chest CT findings in asymptomatic cases was 62%, while it was 90% in those who developed symptoms.[415] Some patients may present with a normal chest finding despite a positive RT-PCR.[416] Also, results of RT-PCR testing may be false-negative, so patients with typical CT findings should have repeat RT-PCR testing to confirm the diagnosis.[417]

Typical features

- The most common findings are ground-glass opacity, either in isolation or coexisting with other findings such as consolidation, interlobular septal thickening, or crazy-paving pattern. The most

common distribution pattern is bilateral, peripheral/subpleural, posterior distribution of the opacities, with a lower lobe predominance. Extensive/multilobar involvement with consolidations is more common in older patients and those with severe disease.[418]

- CT scan generally shows an increase in the size, number, and density of ground-glass opacities in the early follow-up period, with a progression to mixed areas of ground-glass opacities, consolidations, and crazy paving peaking at day 10 to 11, before gradually resolving or persisting as patchy fibrosis.[418]
- A small comparative study found that patients with COVID-19 are more likely to have bilateral involvement with multiple mottling and ground-glass opacity compared with other types of pneumonia.[419]
- Children frequently have normal or mild CT chest findings. The most common signs in children are patchy ground-glass opacity and, less frequently, nonspecific patchy shadows, areas of consolidation, and a halo sign. Abnormalities are more common in the lower lobes and are predominantly unilateral. Pleural effusion is rare. Children may have signs of pneumonia on chest imaging despite having minimal or no symptoms.[420]

#### Atypical features

- Pulmonary vascular enlargement, interlobular or intralobular septal thickening, adjacent pleural thickening, air bronchograms, subpleural lines, crazy-paving pattern, bronchus distortion, bronchiectasis, vacuolar retraction sign, and halo sign are atypical features. Pleural effusion, pericardial effusion, cavitation, pneumothorax, and mediastinal lymphadenopathy have also been reported rarely.[418]

The WHO recommends chest imaging in the following scenarios:[410]

- Symptomatic patients with suspected COVID-19 when RT-PCR is not available, RT-PCR test results are delayed, or initial RT-PCR testing is negative but there is a high clinical suspicion for COVID-19 (for diagnosis)
- Patients with suspected or confirmed COVID-19 who are not currently hospitalized and have mild symptoms (to decide on hospital admission versus home discharge)
- Patients with suspected or confirmed COVID-19 who are not currently hospitalized and have moderate to severe symptoms (to help decide on regular ward admission versus intensive care unit admission)
- Patients with suspected or confirmed COVID-19 who are currently hospitalized and have moderate to severe symptoms (to inform therapeutic management).

## Emerging tests

### Reverse transcription loop-mediated isothermal amplification

- Reverse transcription loop-mediated isothermal amplification (RT-LAMP) assays are an emerging test to detect SARS-CoV-2 viral RNA. While assays are simple and quick, there is less evidence for their use. Assays for SARS-CoV-2 have been developed and are being evaluated.[421] [422] [423]

### Lung ultrasound

- Lung ultrasound is used as a diagnostic tool in some centers as an alternative to chest x-ray and chest CT. Although there is only very low-certainty evidence supporting its diagnostic accuracy, it might be helpful as a supplemental or alternate imaging modality.[410] It has the advantages

of portability, bedside evaluation, reduced healthcare worker exposure, easier sterilization process, absence of ionizing radiation exposure, and repeatability during follow-up. It may also be more readily available in resource-limited settings. However, it also has some limitations (e.g., it is unable to discern chronicity of a lesion) and other imaging modalities may be required. B-lines are the prominent pattern in patients with COVID-19, occurring with a pooled frequency of 97%. Pleural line abnormalities are also common, with a pooled frequency of 70%. While these findings are not specific for COVID-19, they increase the likelihood of disease in the context of a characteristic clinical presentation. Other findings include consolidations, pleural thickening, and pleural effusion.[424] May be used in pregnant women and children.[425] [426]

- [BSTI: lung ultrasound (LUS) for COVID-19 patients in critical care areas]

#### Viral isolation

- Viral isolation is not recommended as a routine diagnostic procedure. All procedures involving viral isolation in cell culture require trained staff and biosafety level 3 (BSL-3) facilities.[345]

## Risk factors

### Strong

#### residence/work/travel in location with high risk of transmission

- People residing or working in an area with a high risk of transmission (e.g., closed residential settings, humanitarian setting), people residing in or traveling to an area with community transmission, and people working in a health setting (including within health facilities and households) at any time within the 14 days prior to symptom onset are at higher risk of infection.[153]

#### contact with probable or confirmed case

- A contact is a person who has experienced any one of the following exposures during the 2 days before and the 14 days after the onset of symptoms of a probable or confirmed case: face-to-face contact with a probable or confirmed case within 3 feet (1 meter) and for at least 15 minutes; direct physical contact with a probable or confirmed case; direct care for a patient with probable or confirmed COVID-19 without using recommended personal protective equipment; or other situations as indicated by local risk assessments.[153]

#### older age

- Older age is a risk factor for infection.[154] Data from a cross-sectional study in the UK indicate that people aged 40 to 64 years are at greatest risk of infection, followed by patients 75 years and older, and then people aged 65 to 74 years.[155] The risk of severe illness in adults increases with age, with older people (ages 65 years and older) at highest risk.[156] [157] The highest mortality rate has been observed in patients 80 years and older.[158] In the US, patients  $\geq 65$  years accounted for 31% of all cases, 45% of hospitalizations, 53% of intensive care unit admissions, and 80% of deaths, with the highest incidence of severe outcomes in patients ages  $\geq 85$  years.[7] While age is an independent risk factor, the risk in older people is also partly related to the likelihood that older adults are more likely to have comorbidities.

#### residence in a long-term care facility

- Widespread transmission has been reported in long-term care facilities.[95] People who live in a nursing home or long-term care facility are at higher risk for severe illness.[157] Care home residents

represent approximately one third of the total number of deaths in England and Wales; other countries have reported a similar experience. This is likely due to shortages in personal protective equipment, a vulnerable population, and a lack of testing.[159] More than one third of care homes in England have had cases.[160] A study across four nursing homes in the UK found that 26% of residents died over a 2-month period, with all-cause mortality increasing by 203% compared with previous years. Approximately 40% of residents tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and of these, 43% were asymptomatic and 18% had atypical symptoms.[161]

### male sex

- Male sex is a risk factor for infection, more severe disease, worse prognosis, and mortality.[162] Data from a cross-sectional study in the UK found that the adjusted odds of a positive test were greater in males (18.4%) compared with females (13.3%).[155] It has been hypothesized that this may be due to the presence of androgens, a lower level of SARS-CoV-2 antibodies compared with females, or women mounting a stronger immune response compared with men; however, further research is required.[163] [164] [165]

### ethnicity

- People from Black, Asian, and minority ethnic (BAME) groups are at a higher risk of infection and worse outcomes, including an increased risk of mortality, compared with the general population. The reasons for this are unclear and require further research.[166] Data from a cross-sectional study in the UK found that South Asian and Black patients had 1.93 and 1.47 the odds of suspected infection, respectively.[167] The average age of patients from ethnic minorities was significantly lower than that of White patients.[168] Ethnic minorities in the UK (including South Asian, East Asian, Black, and other ethnic minorities) admitted to hospital were more likely to be admitted to intensive care and require invasive mechanical ventilation compared with White patients, despite similar disease severity at admission and being younger with fewer comorbidities.[169] There is also evidence from the US that supports this. Age-adjusted data from the Centers for Disease Control and Prevention (as of 25 June) show that non-Hispanic American Indian, Alaska Native, and non-Hispanic Black people have approximately 5 times the rate of hospitalizations of non-Hispanic White people, and Hispanic or Latino people have approximately 4 times the rate of hospitalizations of non-Hispanic White people.[170] However, a cohort study of over 11,000 patients across 12 states in the US found there was no difference in all-cause, in-hospital mortality between Black and White patients after adjusting for sociodemographic factors and comorbidities (e.g., age, sex, insurance).[171] In a study of over 10,000 deceased patients in the US, 35% of Hispanic and 30% of non-White decedents were ages <65 years, compared with 13% of White, non-Hispanic decedents.[172]

### presence of comorbidities

- People with comorbidities are at higher risk for severe illness and mortality.[173] The more comorbidities a person has, the greater their risk for severe illness.[174] In the US, approximately 90% of hospitalized patients had at least one reported underlying medical condition (as of 12 September 2020).[175] The most prevalent comorbidities in adults with COVID-19 are hypertension, diabetes, chronic respiratory disease, cardiovascular disease, and other chronic diseases such as cancer.[176] In a prospective observational cohort study of more than 20,000 hospitalized patients in the UK, the most common comorbidities were chronic cardiac disease (31%), uncomplicated diabetes (21%), nonasthmatic chronic pulmonary disease (18%), and chronic kidney disease (16%).[6] Similarly, in the US the most common comorbidities were cardiovascular disease (32%), diabetes (30%), and chronic lung disease (18%). Hospitalizations were six times higher and deaths were 12 times

higher in patients with comorbidities compared with those without.[177] It has been estimated that approximately 56% of adults in the US are at risk for requiring hospitalization from COVID-19 because of the presence of at least one comorbidity. These underlying conditions are associated with modifiable risk factors, which, if improved through lifestyle changes, may improve a person's risk status.[178]

- Among 345 pediatric cases with information on underlying conditions, 23% had at least one underlying condition, most commonly chronic lung disease, cardiovascular disease, or immunosuppression.[179] Approximately 39% of hospitalized children had an underlying condition in another study. The most prevalent comorbidities were asthma, neurologic disorders, diabetes, obesity, cardiovascular disease, and malignancy/hematologic conditions.[180]
- Around 32% of young adults (ages 18-25 years) in the US had underlying conditions that put them at risk for severe disease including heart conditions, diabetes, asthma, immune conditions, liver conditions, and obesity. Smoking (including e-cigarette use) in the past 30 days also increased the risk. The rate of young adults at risk for severe disease decreased to 16% when considering nonsmokers only.[181]

### cardiovascular disease

- People with serious heart conditions (e.g., heart failure, coronary artery disease, cardiomyopathy, pulmonary hypertension) are at increased risk of severe illness.[174] Cardiovascular disease is associated with a 3-fold increased odds of severe infection, and an 11-fold increase in all-cause mortality.[182]

### hypertension

- People with hypertension may be at increased risk of severe illness.[174] Hypertension has been associated with increased poor composite outcome, including mortality, severe disease, acute respiratory distress syndrome, need for intensive care admission, and disease progression.[183] Patients with hypertension have a 2.27-fold higher risk of severe disease, and a 3.48-fold higher risk of fatality compared with patients without hypertension.[184]

### diabetes

- People with type 2 diabetes are at increased risk of severe illness. People with type 1 diabetes or gestational diabetes may also be at increased risk of severe illness; however, evidence is limited for these patient groups.[174] The pooled prevalence of diabetes in COVID-19 patients is approximately 15%.[185] Diabetes is associated with an increased risk of disease progression, intensive care admission, acute respiratory distress syndrome, mechanical ventilation, and mortality.[186] [187] The risk of intensive care admission and mortality is significantly higher in patients with diabetes compared with those without diabetes (pooled risk ratio of 1.88 and 1.61, respectively).[185] Risk factors for poor prognosis and higher mortality in patients with type 1 or type 2 diabetes include older age, male sex, non-White ethnicity, socioeconomic deprivation, renal impairment, history of stroke or heart failure, higher glycosylated hemoglobin (HbA1c) levels, higher body mass index, elevated C-reactive protein, diabetic ketoacidosis, and insulin use.[188] [189] [190] However, HbA1c levels were not associated with mortality in a large US cohort of hospitalized patients with diabetes and COVID-19, while insulin treatment and obesity were strong and independent risk factors for in-hospital mortality.[191] Hyperglycemia is also an independent risk factor for poor prognosis in hospitalized patients with or without known diabetes.[192] [193] One third of all deaths in hospitalized patients in England occur in patients with diabetes. People with type 1 diabetes have 3.50 times the odds of dying in hospital with COVID-19, while people with type 2 diabetes have 2.03 times the odds.[194] Patients

with newly diagnosed diabetes have a higher risk of all-cause mortality compared with patients with known diabetes, hyperglycemia, or normal glucose.[195] The poor prognosis in these patients is likely due to the syndromic nature of diabetes, with factors such as hyperglycemia, older age, and the presence of comorbidities (e.g., obesity, hypertension, cardiovascular disease) all contributing to the increased risk.[196]

### chronic respiratory disease

- There is no clear evidence that people with asthma or chronic obstructive pulmonary disease (COPD) are at higher risk of infection.[197] [198] People with COPD (including emphysema and chronic bronchitis) are at increased risk of severe illness.[174] COPD is associated with a 5-fold increased risk of severe infection.[199] People with moderate to severe asthma may be at increased risk of severe illness; however, evidence is limited.[174] There is no statistically significant association between asthma and a higher risk of mortality in patients with COVID-19.[200] Asthma prevalence among hospitalized COVID-19 patients appeared to be similar to the asthma prevalence in the general population in one study, and asthma was not an independent risk factor for intubation.[201] People with other chronic lung diseases (e.g., cystic fibrosis, idiopathic pulmonary fibrosis) may be at increased risk of severe illness; however, the evidence is limited.[174] There are no data on whether pediatric respiratory diseases (including childhood asthma) are risk factors for infection or severity.[202]

### chronic kidney disease

- People with chronic kidney disease may be at higher risk of infection. Data from a cross-sectional study in the UK found that the adjusted odds of a positive test were greater in patients with chronic kidney disease (32.9%) compared with those without (14.4%).[155] People with chronic kidney disease are also at increased risk of severe illness.[174] The prevalence of preexisting chronic kidney disease in COVID-19 patients was 5.2% (2.3% for end-stage kidney disease), and is an independent risk factor for developing acute kidney injury as a complication.[203]

### malignancy

- People with cancer are at a higher risk of infection, likely due to immunosuppressive treatments and/or recurrent hospital visits.[204] People with cancer are also at increased risk of severe illness.[174] The overall pooled prevalence of cancer in COVID-19 patients is approximately 2.3%, and it is significantly associated with severe disease.[205] Patients with cancer are 76% more likely to get severe disease compared with those without cancer.[206] They also have an increased risk of worse clinical outcomes including intensive care unit admission and all-cause mortality (particularly those with metastatic disease, hematologic cancer, or lung cancer), and appear to deteriorate more quickly compared with patients without cancer.[207] [208] Patients with hematologic malignancies (in particular, leukemia) have a higher risk of severe or critical disease and a high mortality rate compared with patients with solid tumors.[209] [210] The odds ratio of intensive care admission rates and mortality rates between cancer and noncancer groups was 2.88 and 2.25, respectively.[211] Factors associated with an increased mortality rate in adults include older age, male sex, smoking status, number of comorbidities, Eastern Cooperative Oncology Group performance status of 2 or more, receiving chemotherapy within 4 weeks before symptom onset, cancer surgery, and active cancer.[212] [213] [214] [215] The all-cause mortality rate in patients with cancer is significantly associated with increasing age.[210] Children with cancer may be no more vulnerable to infection compared with children without cancer. Limited data show that the overall morbidity in pediatric patients with cancer is low, with only 5% requiring hospitalization for symptoms.[216] Pooled case fatality rates of between

6.8% and 21% have been reported in adults with cancer, although these rates should be interpreted with caution.[217]

## obesity

- People with obesity are at increased risk of severe illness.[174] A pooled analysis found that people with obesity are at a 46% higher risk of infection, a 113% higher risk of hospitalization, a 74% higher risk of intensive care admission, and 48% higher risk of mortality.[218] Patients with a body mass index  $\geq 30$  kg/m<sup>2</sup> have a 2.35-fold risk for critical disease, and a 2.68-fold risk of in-hospital mortality compared with patients with a body mass index  $< 30$  kg/m<sup>2</sup>. [219] Obesity plays a significant role in the risk of death from COVID-19, particularly in males and younger people (<60 years of age).[220] Increased body mass index is a significant risk factor for severe disease in pregnant women.[221] Obesity was the most common comorbidity in children, and was significantly associated with mechanical ventilation in children 2 years and older in a single-center retrospective study in New York.[222]

## sickle cell disease

- People with sickle cell disease are at increased risk of severe illness.[174] Among 178 patients with sickle cell disease and COVID-19 in the US (mean patient age <40 years), 69% were hospitalized, 11% were admitted to intensive care, and 7% died.[223] Infection can cause acute chest syndrome in patients with sickle cell disease.[224] [225]

## solid organ transplant

- People with an immunocompromised state from solid organ transplant are at increased risk of severe illness.[174] Organ transplant recipients may be at higher risk of severe illness or complications, more rapid clinical progression, and a prolonged clinical course compared with the general population due to chronic immunosuppression and the presence of coexisting conditions.[226] [227] [228] [229] [230] [231] Hospitalization and mortality rates in liver transplant recipients are disproportionately high compared with nontransplant patients regardless of age or time after transplant. Older age and diabetes are significant risk factors for death among these patients.[232]

## smoking

- People who are current or former smokers may be at increased risk of severe illness; however, evidence is limited.[174] Current smokers have an increased risk of severe or critical disease. Patients with any smoking history have a significantly increased risk of severe or critical disease, in-hospital mortality, disease progression, and need for mechanical ventilation.[233] This may be due to increased airway expression of the angiotensin-converting enzyme-2 receptor in smokers.[234] The World Health Organization has reviewed the available evidence and concluded that smoking is associated with increased severity of disease and death in hospitalized patients.[235]

## cerebrovascular disease

- People with cerebrovascular disease may be at increased risk of severe illness; however, evidence is limited.[174] The pooled prevalence of preexisting cerebrovascular disease in COVID-19 patients is 4.4%. Patients with preexisting cerebrovascular disease have 2.67-fold higher odds of poor outcomes including intensive care admission, mechanical ventilation, and mortality.[236]

## chronic liver disease

- People with chronic liver disease, especially cirrhosis, may be at increased risk of severe illness; however, evidence is limited.[174] The prevalence of chronic liver disease in COVID-19 patients is

approximately 3%. The presence of chronic liver disease is associated with more severe disease and overall mortality.[237] The 30-day mortality rate is higher in patients with cirrhosis, with the main causes of death being respiratory complications and sudden worsening of liver function leading to end-stage liver disease.[238]

### dyslipidemia

- Dyslipidemia appears to be associated with an increased risk of severe disease according to one meta-analysis.[239]

### metabolic dysfunction-associated fatty liver disease

- Patients with severe COVID-19 may be more likely to have metabolic dysfunction-associated fatty liver disease (MAFLD; also called nonalcoholic fatty liver disease) compared with patients who have nonsevere COVID-19.[240] MAFLD is associated with a 4- to 6-fold increase in severity of COVID-19.[241] Severity of COVID-19 has been associated with younger age (<60 years) and intermediate or high fibrosis-4 (FIB-4) scores in patients with MAFLD.[242] [243]

### surgery

- Surgical mortality and complications are higher in patients with COVID-19 compared with patients without COVID-19.[244] A retrospective study of 34 patients in China who underwent elective surgeries during the incubation period of COVID-19 found that all patients developed pneumonia after surgery. Approximately 44% of these patients required admission to the intensive care unit, and 20% died.[245] Postoperative pulmonary complications occur in half of patients with perioperative SARS-CoV-2 infection, and are associated with higher mortality, particularly in men and those ages 70 years and over.[246]

### pregnancy

- Pregnant women may be at increased risk of severe illness and adverse pregnancy outcomes.[174] According to an analysis of 8200 infected pregnant women, pregnant women were more likely to be hospitalized, to be admitted to the intensive care unit, and to receive mechanical ventilation compared with nonpregnant women; however, mortality rates did not differ.[20]

### immunosuppression

- People who are immunocompromised (e.g., blood or bone marrow transplant, immune deficiencies, prolonged use of corticosteroids or other immunosuppressant medications) may be at increased risk of severe illness; however, evidence is limited.[174] Patients with inflammatory bowel disease who were on long-term biologics or other immunomodulatory therapies did not have a higher risk of poor outcomes; however, recent corticosteroid use may be related to worse outcomes.[247] Glucocorticoid exposure of  $\geq 10$  mg/day (prednisone) has been associated with a higher odds of hospitalization in patients with rheumatologic disease.[248] Also see HIV infection, below.

### Weak

#### air pollution

- Evidence suggests that there may be an association between long-term exposure to ambient air pollution and COVID-19.[249] [250] The highest numbers of cases were recorded in the most polluted regions of Italy, with patients presenting with more severe disease requiring intensive care. The mortality was 2-fold higher in polluted regions compared with other regions.[251] One study found that of deaths from COVID-19 across 66 administrative regions in Italy, Spain, France, and Germany, 78%

of deaths occurred in just five regions, and these regions were the most polluted in terms of nitrogen dioxide levels.[252] A preprint study from Harvard University found that people who live in US regions with high levels of air pollution were more likely to die from COVID-19 than those who live in less polluted areas. The researchers found that an increase of 1 microgram/m<sup>3</sup> in fine particulate matter is associated with an 8% increase in the COVID-19 death rate.[253]

### climate and latitude

- Distribution of community outbreaks along restricted latitude, temperature, and humidity measurements are consistent with the behavior of a seasonal respiratory virus.[254] Evidence suggests that cold and dry conditions may increase transmission, and warm and humid conditions may reduce the rate of infections; however, evidence is not yet sufficient to prove causation.[255] [256] However, there is other evidence that suggests ambient temperature has no significant impact on transmission, especially during the pandemic stage of an emerging pathogen.[257] [258] [259] Further research is required on how weather conditions influence transmission as colder temperatures have been associated with increased transmission of other coronaviruses. Higher latitude may also be associated with an increased risk of cases and deaths in some countries.[260] A positive correlation has been found between lower death rates and a country's proximity to the equator, suggesting a correlation between sunlight exposure (and vitamin D levels) and reduced mortality.[261]

### residence in urban or deprived areas

- Data from a cross-sectional study in the UK found that the adjusted odds of a positive test were greater in people living in urban areas (26.2%) compared with people living in rural areas (5.6%), and in people living in more deprived areas (29.5%) compared with people living in less deprived areas (7.7%).[155]

### vitamin D deficiency

- A single-center, retrospective cohort study suggests that vitamin D deficiency plays a role in the risk of infection.[262] A population-based study in Israel found that patients who tested positive for COVID-19 had significantly lower plasma vitamin D levels compared with those who tested negative. Univariate analysis demonstrated an association between low plasma vitamin D level and increased likelihood of hospitalization. The study concluded that low plasma vitamin D level appears to be an independent risk factor for COVID-19 infection and for hospitalization.[263] A small retrospective observational preprint study (not peer reviewed) also suggests a link between vitamin D insufficiency and COVID-19 severity.[264] Further research is needed.[265] [266] [267] [268]

### ACE inhibitor/angiotensin-II receptor antagonist use

- There was originally concern that people on these drugs may be at increased risk of infection or more severe disease due to upregulation of angiotensin-converting enzyme-2 (ACE2) receptor expression.[269] However, high-certainty evidence suggests that use of these drugs is not associated with severe disease, and moderate-certainty evidence suggests that there is no association between the use of these medications and a positive SARS-CoV-2 test result among symptomatic patients.[270] [271] Despite this reassuring evidence, another meta-analysis found that the use of angiotensin-II receptor antagonists, and not ACE inhibitors, may augment the risk of SARS-CoV-2 infection in adults <60 years of age.[272] A prospective cohort study of over 19,000 patients in England found that these drugs were associated with a significantly reduced risk of COVID-19, and were not associated with an increased risk of intensive care. However, variations between ethnic groups raise the possibility of ethnic-specific effects.[273] The UK National Institute for Health and Care Excellence states that

conclusion cannot be drawn on whether these drugs increase or decrease the risk of developing COVID-19 or severe disease based on the current available evidence.[274] Professional societies recommend that patients who are already on these drugs continue to take them.[275] [276] [277]

### statin use

- There is concern that people on these drugs may be at increased risk of infection or more severe disease as statins have been shown to increase the expression of ACE2 in laboratory animals, and may promote the activation of the inflammatory pathway in acute respiratory distress syndrome leading to more severe disease.[269] However, a retrospective study of nearly 14,000 patients found that statin use was associated with a lower risk of all-cause mortality in patients with COVID-19, possibly due to the immunomodulatory effects of statins. A meta-analysis of four retrospective studies also suggests a reduced risk for fatal or severe disease among statin users.[278] Further research into the potential therapeutic or detrimental effects of statins is required.[279]

### proton-pump inhibitor use

- Proton-pump inhibitors (PPIs) are known to increase the risk of infections due to hypochlorhydria. There is evidence of an independent, dose-response relationship between the use of antisecretory medications and COVID-19 positivity. People taking PPIs had significantly increased odds for reporting a positive COVID-19 test when compared with those not taking PPIs. People taking H2 antagonists were not at elevated risk.[280] Patients taking PPIs may also be at increased risk of severe clinical outcomes.[281]

### HIV infection

- It is still unclear whether HIV infection influences infection and disease course. However, males affected by antiretroviral therapy-related complications may be at greater risk of severe disease.[282]

### autoimmune disease

- Autoimmune disease, in general, does not appear to be associated with a higher risk of infection.[283] [284] Patients with autoimmune rheumatic disease may be more susceptible to infection compared with the general population, although data are scarce.[285] Autoimmune disease has been associated with a slightly increased risk of disease severity and mortality; however, this was not statistically significant.[286] Risk of mortality appears to be associated with older age and the presence of comorbidities even in patients with autoimmune disease, rather than the autoimmune disease itself or use of immunosuppressive medications.[287] In patients with multiple sclerosis, neurologic disability, age, and obesity were risk factors for severe disease.[288] Weak evidence suggests that people with inflammatory bowel disease may be somewhat protected from infection, likely due to their ongoing treatment for the condition.[289] Further research is required as there is concern about the risk of infection in these patients.

### neurologic conditions

- People with neurologic conditions (e.g., dementia) may be at increased risk of severe illness; however, evidence is limited.[174]

### thalassemia

- People with thalassemia may be at increased risk of severe illness; however, evidence is limited.[174]

## children with certain underlying conditions

- Children may be at increased risk of severe illness if they have certain conditions (e.g., obesity, diabetes, asthma and chronic lung disease, immunosuppression); are medically complex; have serious genetic, neurologic, or metabolic disorders; or have congenital heart disease. However, evidence is limited.[174]

## blood group A#

- People with blood group A appear to be at increased risk of infection, while people with blood group O have a decreased risk (blood groups B and AB were not significantly associated with infection).[290] A genome-wide association study found that patients with blood group A are at 45% increased risk of respiratory failure compared with other blood groups. It also found a protective effect in blood group O. Two chromosomal loci were associated with respiratory failure, and one of these coincided with the ABO blood group locus.[291]

## gut dysbiosis

- There is some emerging evidence that gut microbiota dysfunction may be implicated in the pathogenesis of COVID-19, although this is yet to be confirmed. Patients appear to have a depletion of beneficial commensals (*Eubacterium ventriosum*, *Faecalibacterium prausnitzii*, *Roseburia* and Lachnospiraceae taxa) and an overgrowth of opportunistic pathogens (*Clostridium hathewayi*, *Actinomyces viscosus*, *Bacteroides nordii*) during hospitalisation. Gut microbiome configuration has been associated with disease severity.[292] [293] [294]

# History & examination factors

## Key diagnostic factors

### fever (common)

- Reported in approximately 77% of patients.[106] In one case series, only 44% of patients had a fever on presentation, but it developed in 89% of patients after hospitalization.[427] The course may be prolonged and intermittent, and some patients may have chills/rigors. In children, fever may be absent or brief and rapidly resolving.[428]

### cough (common)

- Reported in approximately 68% of patients.[106] The cough is usually dry; however, a productive cough has been reported in some patients.

### dyspnea (common)

- Reported in approximately 38% of patients.[106] Median time from onset of symptoms to development of dyspnea is 5 to 8 days.[31] [32] [429] It is less common in children, but the most common sign in neonates.[346] May last weeks after initial onset of symptoms. Wheeze has been reported in 17% of patients.[430]

### altered sense of smell/taste (common)

- Olfactory dysfunction (anosmia/hyposmia) has been reported in approximately 41% of patients, and gustatory dysfunction (ageusia/dysgeusia) has been reported in approximately 35% of patients.[106] Prevalence appears to be higher in European studies.[431] May be an early symptom before the onset of other symptoms, or may be the only symptom in patients with mild to moderate

illness.[432] Complete resolution or improvement in symptoms was reported in 89% of patients 4 weeks after onset.[433]

## Other diagnostic factors

### fatigue (common)

- Reported in approximately 30% of patients.[106] Patients may also report malaise. Fatigue and exhaustion may be extreme and protracted, even in patients with mild disease.

### myalgia or arthralgia (common)

- Reported in approximately 17% (myalgia) and 11% (arthralgia) of patients.[430]

### sputum production/expectoration (common)

- Reported in approximately 18% of patients.[106]

### chest tightness (common)

- Reported in approximately 22.9% of patients.[378]

### gastrointestinal symptoms (common)

- Reported in 20% of patients. The weighted pooled prevalence of specific symptoms is as follows: loss of appetite 22.3%; diarrhea 2.4%; nausea/vomiting 9%; and abdominal pain 6.2%. Gastrointestinal symptoms appear to be more prevalent outside of China, although this may be due to increased awareness and reporting of these symptoms as the pandemic progressed.[434] Gastrointestinal symptoms are not associated with an increased likelihood for testing positive for COVID-19; however, anorexia and diarrhea, when combined with loss of smell/taste and fever, were 99% specific for COVID-19 infection in one prospective case-control study.[435] Children may present with gastrointestinal symptoms more commonly than adults, particularly newborns and infants, and these may be the only symptom.[346] Hematochezia has been reported.[436]

### sore throat (common)

- Reported in approximately 16% of patients.[106] Usually presents early in the clinical course.

### headache (common)

- Reported in approximately 16% of patients.[106]

### dizziness (common)

- Reported in approximately 11% of patients.[430]

### neurologic symptoms (common)

- Confusion has been reported in approximately 11% of patients.[430] Prevalence of confusion/delirium and agitation is high (65% and 69%, respectively) in patients in the intensive care unit.[437] Delirium is associated with an increased risk of mortality, and rapid onset may indicate clinical deterioration.[438] Anxiety, depression, and sleep problems have also been reported.[32]

### ocular symptoms (common)

- Reported in 11.2% of patients. The most common ocular symptom is unilateral or bilateral conjunctivitis. Other reported symptoms include ocular pain, dry eye, and floaters. Most symptoms are mild and last for 4 to 14 days with no complications. Prodromal symptoms occur in 12.5%

of patients.[439] Mild ocular symptoms (e.g., conjunctival discharge, eye rubbing, conjunctival congestion) were reported in 22.7% of children in one cross-sectional study. Children with systemic symptoms were more likely to develop ocular symptoms.[440]

### **rhinorrhea/nasal congestion (uncommon)**

- Rhinorrhea has been reported in approximately 8% of patients, and nasal congestion has been reported in approximately 5% of patients.[430]

### **chest pain (uncommon)**

- Reported in approximately 7% of patients.[430] May indicate pneumonia.

### **cutaneous symptoms (uncommon)**

- The pooled prevalence of overall cutaneous lesions is 5.7%. The most common symptoms are a viral exanthem-like presentation (4.2%), maculopapular rash (3.8%), and vesiculobullous lesions (1.7%). Other manifestations include urticaria, chilblain-like lesions, livedo reticularis, and finger/toe gangrene.[441] In the UK COVID Symptom Study, 17% of respondents reported rash as the first symptom of disease, and 21% of respondents reported rash as the only clinical sign.[442] It is unclear whether skin lesions are from viral infection, systemic consequences of the infection, or drugs the patient may be on. Further data is required to better understand cutaneous involvement.

### **hemoptysis (uncommon)**

- Reported in approximately 2% of patients.[430] May be a symptom of pulmonary embolism.[443]

### **bronchial breath sounds (uncommon)**

- May indicate pneumonia.

### **tachypnea (uncommon)**

- May be present in patients with acute respiratory distress.

### **tachycardia (uncommon)**

- May be present in patients with acute respiratory distress.

### **cyanosis (uncommon)**

- May be present in patients with acute respiratory distress.

### **crackles/rales on auscultation (uncommon)**

- May be present in patients with acute respiratory distress.

## Diagnostic tests

### 1st test to order

Test	Result
<p><b>real-time reverse transcription polymerase chain reaction (RT-PCR)</b></p> <ul style="list-style-type: none"> <li>• Order a RT-PCR for SARS-CoV-2 in patients with suspected infection whenever possible (see the Criteria section).[345]</li> <li>• Base decisions about who to test on clinical and epidemiologic factors.[345] Consult local health authorities for guidance as testing priorities depend on local recommendations and available resources.</li> <li>• In the UK, testing is recommended in: (1) people in the community with symptoms of new continuous cough, high temperature, or altered sense of smell/taste; (2) people requiring hospital admission and who have clinical or radiologic evidence of pneumonia, or acute respiratory distress syndrome, or influenza-like illness, or altered sense of smell/taste in isolation or in combination with any other symptoms.[343] [383]</li> <li>• In the US, testing is recommended in: (1) people with symptoms, even if they are mild; (2) people who are asymptomatic and have been in close contact for at least 15 minutes with a person with documented infection; (3) people who are asymptomatic and have not been in close contact for at least 15 minutes with a person with documented infection only if required by a healthcare provider or public health official.[384]</li> <li>• The optimal specimen for testing depends on the clinical presentation and the time since symptom onset. The World Health Organization recommends upper respiratory specimens (nasopharyngeal and/or oropharyngeal swabs) for early-stage infections, especially asymptomatic or mild cases, and lower respiratory specimens (sputum and/or endotracheal aspirate or bronchoalveolar lavage in patients with more severe respiratory disease) for later-stage infections or patients in whom there is a strong suspicion for infection and their upper respiratory tract specimen test was negative. Other specimens (e.g., nasal mid-turbinate swab, anterior nares swab, nasopharyngeal/nasal wash/aspirate, saliva, fecal) may be recommended in some circumstances; consult local guidance.[345] [389]</li> <li>• A positive RT-PCR result confirms SARS-CoV-2 infection. If the result is negative, and there is still a clinical suspicion of infection (e.g., an epidemiologic link, typical x-ray findings, absence of another etiology), resample the patient and repeat the test. A positive result confirms infection. If the second test is negative, consider serologic testing (see below).[345]</li> <li>• Limitations of testing: RT-PCR detects viral RNA but it is not fully understood how that represents infectious virus, which ultimately could lead to restrictions for people who do not present an infection risk.[391] The pooled sensitivity is 86%, and the pooled specificity is 96%. Accuracy depends on the prevalence of the disease in a given population; the lower the prevalence of disease, the lower the post-test probability.[393] Interpreting the test result also depends on the accuracy of the test, and the pretest probability (or estimated risk of disease) before testing.[394] False-positive results are more likely when the prevalence is moderate to low, and can be caused by a laboratory error or a cross-reaction with antibodies formed by current</li> </ul>	<p><b>positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral RNA; may be positive for influenza A and B viruses and other respiratory pathogens</b></p>

Test	Result
<p>and past exposure to seasonal human coronavirus infections (e.g., common cold).[396] [397]</p> <ul style="list-style-type: none"> <li>Also collect nasopharyngeal swabs to rule out influenza and other respiratory infections according to local guidance. It is important to note that coinfections can occur, and a positive test for a non-COVID-19 pathogen does not rule out COVID-19.[2] [390] A single-test multiplex assay to diagnose infection caused by influenza A, influenza B, and SARS-CoV-2 is available in the US.[444]</li> </ul>	
<p><b>pulse oximetry</b></p> <ul style="list-style-type: none"> <li>Order in patients with severe illness.</li> <li>Recommended in patients with respiratory distress and cyanosis.</li> <li>Clinicians should be aware that patients with COVID-19 can develop "silent hypoxia": their oxygen saturations can drop to low levels and precipitate acute respiratory failure without the presence of obvious symptoms of respiratory distress. Only a small proportion of patients have other organ dysfunction, meaning that after the initial phase of acute deterioration, traditional methods of recognizing further deterioration (e.g., National Early Warning Score 2 [NEWS2] scores) may not help predict those patients who go on to develop respiratory failure.[375]</li> </ul>	<p><b>may show low oxygen saturation (SpO<sub>2</sub> &lt;90%)</b></p>
<p><b>ABG</b></p> <ul style="list-style-type: none"> <li>Order in patients with severe illness as indicated to detect hypercarbia or acidosis.</li> <li>Recommended in patients with respiratory distress and cyanosis who have low oxygen saturation (SpO<sub>2</sub> &lt;90%).</li> </ul>	<p><b>may show low partial oxygen pressure</b></p>
<p><b>CBC</b></p> <ul style="list-style-type: none"> <li>Order in patients with severe illness.</li> <li>Lymphopenia, leukocytosis, thrombocytopenia, decreased eosinophils, decreased hemoglobin, and high neutrophil-to-lymphocyte ratio are significantly associated with severe disease, and may be useful for predicting disease progression. Severe cases are more likely to present with lymphopenia and thrombocytopenia, but not leukopenia.[445]</li> <li>Elevated red blood cell distribution width (at admission and increasing during hospitalization) has been associated with a significantly increased risk of mortality in hospitalized patients.[446]</li> <li>Absolute counts of major lymphocyte subsets, particularly CD4+ and CD8+ T-cell counts, are significantly decreased in patients with severe disease.[447]</li> <li>Late-phase thrombocytopenia (i.e., occurring 3 weeks or more after symptom onset) has been reported but is uncommon.[448]</li> </ul>	<p><b>lymphopenia; leukocytosis; leukopenia; thrombocytopenia; decreased eosinophils; decreased hemoglobin</b></p>
<p><b>comprehensive metabolic panel</b></p> <ul style="list-style-type: none"> <li>Order in patients with severe illness.</li> <li>Elevated liver enzymes, total bilirubin, creatinine, and blood urea nitrogen, and hypoalbuminemia are significantly associated with severe disease, and may be useful for predicting disease progression.[445]</li> <li>Hypokalemia has been reported in 54% of patients.[449] Hypocalcemia has been reported in 63% of patients.[450] Other electrolyte derangements may be present.</li> </ul>	<p><b>elevated liver enzymes; elevated total bilirubin; renal impairment; hypoalbuminemia; electrolyte derangements</b></p>
<p><b>blood glucose level</b></p> <ul style="list-style-type: none"> <li>Order in patients with severe illness.</li> </ul>	<p><b>variable</b></p>

Test	Result
<ul style="list-style-type: none"> <li>Uncontrolled hyperglycemia has been shown to worsen prognosis in all patients, not only patients with diabetes.[451] [452] [453]</li> </ul>	
<b>coagulation screen</b> <ul style="list-style-type: none"> <li>Order in patients with severe illness.</li> <li>Elevated D-dimer and prolonged prothrombin time are significantly associated with severe disease, and may be useful for predicting disease progression.[445]</li> <li>The risk of severe disease and mortality is 2-fold and 4-fold higher, respectively, in patients with elevated D-dimer levels.[454] Patients with very high D-dimer levels have an increased risk of thrombosis.[455] [456]</li> </ul>	<b>elevated D-dimer; prolonged prothrombin time; elevated fibrinogen</b>
<b>cardiac biomarkers</b> <ul style="list-style-type: none"> <li>Order in patients with severe illness.</li> <li>Elevated serum troponin I and creatine kinase-myocardial band (CK-MB) are significantly associated with severe disease, and may be useful for predicting disease progression.[445]</li> <li>Other cardiac biomarkers (e.g., brain natriuretic peptide, cardiac troponin T) may also be elevated and are associated with severe disease and worse outcomes.[457] [458]</li> <li>CK-MB has been found to be elevated in mild disease in children. The significance of this is unknown.[381]</li> </ul>	<b>may be elevated</b>
<b>serum C-reactive protein</b> <ul style="list-style-type: none"> <li>Order in patients with severe illness.</li> <li>Elevated C-reactive protein is significantly associated with severe disease, and may be useful for predicting disease progression.[445]</li> </ul>	<b>may be elevated</b>
<b>serum erythrocyte sedimentation rate</b> <ul style="list-style-type: none"> <li>Order in patients with severe illness.</li> <li>Commonly elevated in patients with COVID-19.[379]</li> </ul>	<b>may be elevated</b>
<b>serum lactate dehydrogenase</b> <ul style="list-style-type: none"> <li>Order in patients with severe illness.</li> <li>Elevated serum lactate dehydrogenase is significantly associated with severe disease, and may be useful for predicting disease progression.[445]</li> </ul>	<b>may be elevated</b>
<b>serum interleukin-6 level</b> <ul style="list-style-type: none"> <li>Order in patients with severe illness.</li> <li>Elevated interleukin-6 level is significantly associated with severe disease, and may be useful for predicting disease progression.[445]</li> <li>Less likely to be elevated in children.[459]</li> </ul>	<b>may be elevated</b>
<b>serum procalcitonin</b> <ul style="list-style-type: none"> <li>Order in patients with severe illness.</li> <li>Elevated serum procalcitonin is significantly associated with severe disease, and may be useful for predicting disease progression.[445]</li> <li>Elevated serum procalcitonin may be more common in children.[373]</li> <li>May be elevated in patients with secondary bacterial infection.[31] [32]</li> <li>There is insufficient evidence to recommend routine procalcitonin testing to guide decisions about the use of antibiotics.[460]</li> <li>However, it may be helpful in limiting overuse of antibiotics in patients with COVID-19-related pneumonia.[461]</li> </ul>	<b>may be elevated</b>
<b>serum ferritin level</b>	<b>may be elevated</b>

Test	Result
<ul style="list-style-type: none"> <li>Order in patients with severe illness.</li> <li>May indicate development of cytokine release syndrome.[462]</li> </ul>	
<p><b>serum amyloid A level</b></p> <ul style="list-style-type: none"> <li>Order in patients with severe illness.</li> <li>Levels increase in severe disease; therefore, it may be useful as a biomarker for predicting disease progression.[463]</li> </ul>	<b>may be elevated</b>
<p><b>serum creatine kinase and myoglobin</b></p> <ul style="list-style-type: none"> <li>Order in patients with severe illness.</li> <li>Elevated serum creatine kinase and myoglobin are significantly associated with severe disease, and may be useful for predicting disease progression.[445]</li> </ul>	<b>may be elevated</b>
<p><b>blood and sputum cultures</b></p> <ul style="list-style-type: none"> <li>Collect blood and sputum specimens for culture in patients with severe or critical disease to rule out other causes of lower respiratory tract infection and sepsis, especially patients with an atypical epidemiologic history.[2]</li> <li>Testing is most useful when there is concern for multidrug-resistant pathogens.[461]</li> <li>Specimens should be collected prior to starting empiric antimicrobials if possible.</li> </ul>	<b>negative for bacterial infection</b>
<p><b>chest x-ray</b></p> <ul style="list-style-type: none"> <li>Order in all patients with suspected pneumonia.</li> <li>Unilateral lung infiltrates are found in 25% of patients, and bilateral lung infiltrates are found in 75% of patients.[31] [32] [409]</li> <li>Although chest x-ray appears to have a lower sensitivity compared with chest CT, it has the advantages of being less resource-intensive, associated with lower radiation doses, easier to repeat sequentially, and portable.[410]</li> </ul>	<b>unilateral or bilateral lung infiltrates</b>

## Other tests to consider

Test	Result
<p><b>computed tomography (CT) chest</b></p> <ul style="list-style-type: none"> <li>Consider a CT scan of the chest. Consult local guidance on whether to perform a CT scan. The British Society of Thoracic Imaging (BSTI) recommends CT imaging in patients with clinically suspected COVID-19 who are seriously ill if chest x-ray is uncertain or normal. <a href="#">[BSTI: radiology decision tool for suspected COVID-19]</a> Some institutions in the UK recommend a more pragmatic approach for patients with high clinical suspicion of COVID-19, with chest CT recommended only after two indeterminate or normal chest x-rays in combination with a negative RT-PCR test.<a href="#">[411]</a> The American College of Radiology recommends reserving CT for hospitalized, symptomatic patients with specific clinical indications for CT, and emphasizes that a normal chest CT does not mean that a patient does not have COVID-19 and that an abnormal chest CT is not specific for COVID-19 diagnosis.<a href="#">[412]</a></li> <li>Abnormal chest CT findings have been reported in up to 97% of hospitalized patients.<a href="#">[413]</a> Evidence of pneumonia on CT may precede a positive RT-PCR result for SARS-CoV-2 in some patients.<a href="#">[414]</a> CT imaging abnormalities may be present in asymptomatic patients. The pooled estimate of the rate of positive chest CT findings in asymptomatic cases was 62%, while it was 90% in those who developed symptoms.<a href="#">[415]</a> Some patients may present with a normal chest finding despite a positive RT-PCR.<a href="#">[416]</a> Also, results of RT-PCR testing may be false-negative, so patients with typical CT findings should have repeat RT-PCR testing to confirm the diagnosis.<a href="#">[417]</a></li> <li>The most common findings are ground-glass opacity, either in isolation or coexisting with other findings such as consolidation, interlobular septal thickening, or crazy-paving pattern. The most common distribution pattern is bilateral, peripheral/subpleural, posterior distribution of the opacities, with a lower lobe predominance. Extensive/multilobar involvement with consolidations is more common in older patients and those with severe disease. Pulmonary vascular enlargement, interlobular or intralobular septal thickening, adjacent pleural thickening, air bronchograms, subpleural lines, crazy-paving pattern, bronchus distortion, bronchiectasis, vacuolar retraction sign, and halo sign are atypical features. Pleural effusion, pericardial effusion, cavitation, pneumothorax, and mediastinal lymphadenopathy have also been reported rarely.<a href="#">[418]</a></li> <li>Children frequently have normal or mild CT chest findings. The most common signs in children are patchy ground-glass opacity and, less frequently, nonspecific patchy shadows, areas of consolidation, and a halo sign. Abnormalities are more common in the lower lobes and are predominantly unilateral. Pleural effusion is rare.<a href="#">[420]</a></li> <li>CT scan generally shows an increase in the size, number, and density of ground-glass opacities in the early follow-up period, with a progression to mixed areas of ground-glass opacities, consolidations, and crazy paving peaking at day 10 to 11, before gradually resolving or persisting as patchy fibrosis.<a href="#">[418]</a></li> <li>The positive predictive value was low (1.5% to 30.7%) in low-prevalence regions, and the negative predictive value ranged from 95.4% to 99.8% in one meta-analysis. Pooled sensitivity and specificity were 94% and 37%, respectively.<a href="#">[464]</a> A sensitivity of 96% has been reported in another meta-analysis.<a href="#">[465]</a></li> </ul>	<p><b>ground-glass opacity in isolation or coexisting with other findings (e.g., consolidation, interlobular septal thickening, crazy-paving pattern); bilateral, peripheral/subpleural, posterior distribution with a lower lobe predominance</b></p>

Test	Result
<ul style="list-style-type: none"> <li>In a cohort of over 1000 patients in a hyperendemic area in China, chest CT had a higher sensitivity for diagnosis of COVID-19 compared with initial RT-PCR from swab samples (88% versus 59%). Improvement of abnormal CT findings also preceded change from RT-PCR positivity to negativity in this cohort during recovery. The sensitivity of chest CT was 97% in patients who ultimately had positive RT-PCR results. However, in this setting, 75% of patients with negative RT-PCR results also had positive chest CT findings. Of these patients, 48% were considered highly likely cases, while 33% were considered probable cases.<a href="#">[466]</a> <a href="#">[Fig-2]</a></li> </ul>	
<p><b>serology</b></p> <ul style="list-style-type: none"> <li>Cannot be used as a standalone diagnostic for acute infections; however, may be useful in various settings (e.g, negative molecular testing, diagnosing patients with late presentation or prolonged symptoms, serosurveillance studies).<a href="#">[345]</a> <a href="#">[399]</a></li> <li><a href="#">[BMJ practice pointer: testing for SARS-CoV-2 antibodies]</a></li> <li>The World Health Organization (WHO) recommends collecting a paired serum sample, one specimen in the acute phase and one in the convalescent phase 2 to 4 weeks later, in patients where infection is strongly suspected and the RT-PCR result is negative. Seroconversion or a rise in antibody titers in paired sera help to confirm whether the infection is recent and/or acute. If the initial sample tests positive, this could be due to a past infection that is not related to the current illness. Seroconversion may be faster and more robust in patients with severe disease compared with those with mild disease or asymptomatic infection.<a href="#">[345]</a></li> <li>The Centers for Disease Control and Prevention recommends serologic testing as a method to support the diagnosis of acute infection in patients who present late (i.e., 9 to 14 days after symptom onset) in addition to other viral detection methods (e.g., RT-PCR, antigen detection tests), or patients who present with late complications (e.g., pediatric inflammatory multisystem syndrome in children).<a href="#">[400]</a></li> <li>The Infectious Diseases Society of America recommends serologic testing in the following circumstances: evaluation of patients with a high clinical suspicion for infection when molecular diagnostic testing is negative and at least 2 weeks have passed since symptom onset; evaluation of pediatric inflammatory multisystem syndrome in children; and serosurveillance studies.<a href="#">[401]</a></li> <li>Antibody responses to SARS-CoV-2 typically occur during the first 1 to 3 weeks of illness, with the seroconversion time of IgG antibodies often being earlier than that of IgM antibodies.<a href="#">[402]</a> <a href="#">[403]</a></li> <li>Limitations of testing: serologic testing cannot be used to determine acute infection; results do not indicate the presence or absence of current or previous infection with certainty; reliable diagnosis is often only possible in the recovery phase when opportunities for management or interruption of transmission have passed; cross-reactivity with other coronaviruses, which can result in false-positive results.<a href="#">[345]</a> <a href="#">[400]</a></li> <li>While rapid antibody detection kits have been approved for the qualitative detection of SARS-CoV-2 IgG/IgM antibodies in serum, plasma, or whole blood, the WHO does not recommend the use of these tests outside of research settings as they have not been validated as yet.<a href="#">[405]</a></li> </ul>	<p><b>positive for SARS-CoV-2 virus antibodies; seroconversion or a rise in antibody titers in paired sera</b></p>

Test	Result
<p><b>antigen test</b></p> <ul style="list-style-type: none"> <li>• Rapid diagnostic test. Relies on direct detection of SARS-CoV-2 viral proteins in nasal swabs and other respiratory specimens using a lateral flow immunoassay. Results are usually available in less than 30 minutes. While antigen tests are substantially less sensitive than RT-PCR, they offer the possibility of rapid, inexpensive, and early detection of the most infectious cases in appropriate settings. If used, testing should occur within the first 5 to 7 days following the onset of symptoms. The World Health Organization recommends antigen testing only in certain scenarios where RT-PCR is unavailable or where prolonged turnaround times preclude clinical utility, provided that the test meets the minimum performance requirements of ≥80% sensitivity and ≥97% specificity compared with a RT-PCR reference assay.<a href="#">[407]</a></li> </ul>	<p><b>positive for SARS-CoV-2 virus antigen</b></p>

### Emerging tests

Test	Result
<p><b>reverse transcription loop-mediated isothermal amplification (RT-LAMP)</b></p> <ul style="list-style-type: none"> <li>• A similar process to RT-PCR, but uses constant temperatures and produces more viral DNA compared with RT-PCR. While simple and quick, it is a newer technology and there is less evidence for its use. Assays for SARS-CoV-2 have been developed and are being evaluated.<a href="#">[421]</a> <a href="#">[422]</a> <a href="#">[423]</a></li> </ul>	<p><b>positive for SARS-CoV-2 viral RNA</b></p>
<p><b>lung ultrasound</b></p> <ul style="list-style-type: none"> <li>• Lung ultrasound is used as a diagnostic tool in some centers as an alternative to chest x-ray and chest CT. Although there is only very low-certainty evidence supporting its diagnostic accuracy, it might be helpful as a supplemental or alternate imaging modality.<a href="#">[410]</a></li> <li>• Has the advantages of portability, bedside evaluation, reduced healthcare worker exposure, easier sterilization process, absence of ionizing radiation exposure, and repeatability during follow-up. It may also be more readily available in resource-limited settings. However, it also has some limitations (e.g., it is unable to discern chronicity of a lesion) and other imaging modalities may be required.</li> <li>• B-lines are the prominent pattern in patients with COVID-19, occurring with a pooled frequency of 97%. Pleural line abnormalities are also common with a pooled frequency of 70%. While these findings are not specific for COVID-19, they increase the likelihood of disease in the context of a characteristic clinical presentation. Other findings include consolidations, pleural thickening, and pleural effusion.<a href="#">[424]</a></li> <li>• May be used in pregnant women and children.<a href="#">[425]</a> <a href="#">[426]</a></li> <li>• <a href="#">[BSTI: lung ultrasound (LUS) for COVID-19 patients in critical care areas]</a></li> </ul>	<p><b>B-lines; pleural line abnormalities</b></p>

DIAGNOSIS

## Differential diagnosis

Condition	Differentiating signs / symptoms	Differentiating tests
<b>Community-acquired pneumonia</b>	<ul style="list-style-type: none"> <li>Lack of residence in/travel history to an area with ongoing transmission, or lack of close contact with a suspected/confirmed case of COVID-19 in the 14 days prior to symptom onset.</li> <li>Differentiating COVID-19 from community-acquired bacterial pneumonia is not usually possible from signs and symptoms. However, patients with bacterial pneumonia are more likely to have rapid development of symptoms and purulent sputum. They are less likely to have myalgia, anosmia, or pleuritic pain.[467] [468]</li> </ul>	<ul style="list-style-type: none"> <li>Blood or sputum culture or molecular testing: positive for causative organism.</li> <li>RT-PCR: negative for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral RNA (coinfections are possible).</li> <li>CT chest: centrilobular nodules, mucoid impactions.[469]</li> </ul>
<b>Influenza infection</b>	<ul style="list-style-type: none"> <li>Lack of residence in/travel history to an area with ongoing transmission, or lack of close contact with a suspected/confirmed case of COVID-19 in the 14 days prior to symptom onset.</li> <li>Differentiating COVID-19 from community-acquired respiratory tract infections is not possible from signs and symptoms.</li> <li>Symptoms typically peak during the first 3 to 7 days of illness with influenza, compared with week 2 or 3 of illness with COVID-19.[470]</li> <li>Influenza is more common in children.[470] Children with COVID-19 tend to be older, and are more likely to have comorbidities, fever, gastrointestinal symptoms, headache, and chest pain compared with those with influenza.[471]</li> <li>A small case-control study found that new-onset smell and/or taste disorders were more common among patients with COVID-19</li> </ul>	<ul style="list-style-type: none"> <li>RT-PCR: positive for influenza A or B viral RNA; negative for SARS-CoV-2 viral RNA (coinfections are possible).</li> <li>CT chest: there is emerging evidence that CT can be used for differentiating between influenza and COVID-19. COVID-19 patients are more likely to have rounded or linear opacities, crazy-paving sign, vascular enlargement, and interlobular septal thickening, but less likely to have nodules, tree-in-bud sign, bronchiectasis, and pleural effusion.[473] [474]</li> <li>Inflammatory markers and coagulation screen: there is emerging evidence that inflammatory markers (lactate dehydrogenase, erythrocyte sedimentation rate, C-reactive protein) and coagulation parameters are not as high in patients with influenza compared with COVID-19.[475]</li> </ul>

Condition	Differentiating signs / symptoms	Differentiating tests
	<p>compared with patients with influenza.[472]</p>	
<b>Common cold</b>	<ul style="list-style-type: none"> <li>• Lack of residence in/travel history to an area with ongoing transmission, or lack of close contact with a suspected/confirmed case of COVID-19 in the 14 days prior to symptom onset.</li> <li>• Differentiating COVID-19 from community-acquired respiratory tract infections is not possible from signs and symptoms.</li> </ul>	<ul style="list-style-type: none"> <li>• RT-PCR: positive for causative organism; negative for SARS-CoV-2 viral RNA (coinfections are possible).</li> </ul>
<b>Other viral or bacterial respiratory infections</b>	<ul style="list-style-type: none"> <li>• Lack of residence in/travel history to an area with ongoing transmission, or lack of close contact with a suspected/confirmed case of COVID-19 in the 14 days prior to symptom onset.</li> <li>• Differentiating COVID-19 from community-acquired respiratory tract infections is not possible from signs and symptoms.</li> <li>• Adenovirus and <i>Mycoplasma</i> should be considered in clusters of pneumonia patients, especially in closed settings such as military camps and schools.</li> </ul>	<ul style="list-style-type: none"> <li>• Blood or sputum culture of molecular testing: positive for causative organism.</li> <li>• RT-PCR: negative for SARS-CoV-2 viral RNA (coinfections are possible).</li> </ul>
<b>Aspiration pneumonia</b>	<ul style="list-style-type: none"> <li>• Lack of residence in/travel history to an area with ongoing transmission, or lack of close contact with a suspected/confirmed case of COVID-19 in the 14 days prior to symptom onset.</li> <li>• Differentiating COVID-19 from aspiration pneumonia is not usually possible from signs and symptoms.</li> </ul>	<ul style="list-style-type: none"> <li>• RT-PCR: negative for SARS-CoV-2 viral RNA (coinfections are possible).</li> <li>• CT chest: difficult to distinguish on CT; however, anterior lung involvement may be more suggestive of COVID-19 pneumonia.[476]</li> </ul>
<b>Pneumocystis jirovecii pneumonia</b>	<ul style="list-style-type: none"> <li>• Lack of residence in/travel history to an area with ongoing transmission, or lack of close contact with a suspected/confirmed case of COVID-19 in the 14 days prior to symptom onset.</li> </ul>	<ul style="list-style-type: none"> <li>• Sputum culture: positive for <i>Pneumocystis</i>.</li> <li>• RT-PCR: negative for SARS-CoV-2 viral RNA (coinfections are possible).</li> <li>• CT chest: ground-glass opacity is usually more diffusely distributed with</li> </ul>

Condition	Differentiating signs / symptoms	Differentiating tests
	<ul style="list-style-type: none"> <li>• Differentiating COVID-19 from pneumocystis jirovecii pneumonia is not usually possible from signs and symptoms.</li> <li>• Patients are usually immunocompromised (e.g., HIV positive) and duration of symptoms may be longer.</li> </ul>	a tendency to spare the subpleural regions.[469]
<b>Middle East respiratory syndrome (MERS)</b>	<ul style="list-style-type: none"> <li>• Travel history to the Middle East or contact with a confirmed case of MERS.</li> <li>• Differentiating COVID-19 from MERS is not possible from signs and symptoms.</li> <li>• Initial data suggest that the clinical course of COVID-19 is less severe and the case fatality rate is lower compared with MERS.</li> </ul>	<ul style="list-style-type: none"> <li>• Reverse-transcriptase polymerase chain reaction (RT-PCR): positive for MERS-CoV viral RNA.</li> </ul>
<b>Severe acute respiratory syndrome (SARS)</b>	<ul style="list-style-type: none"> <li>• There have been no cases of SARS reported since 2004.</li> </ul>	<ul style="list-style-type: none"> <li>• RT-PCR: positive for severe acute respiratory syndrome coronavirus (SARS-CoV) viral RNA.</li> </ul>
<b>Avian influenza A (H7N9) virus infection</b>	<ul style="list-style-type: none"> <li>• May be difficult to differentiate based on epidemiologic history as avian influenza H7N9 is endemic in China.</li> <li>• Close contact with infected birds (e.g., farmer or visitor to a live market in endemic areas), or living in an area when avian influenza is endemic.</li> </ul>	<ul style="list-style-type: none"> <li>• RT-PCR: positive for H7-specific viral RNA.</li> </ul>
<b>Avian influenza A (H5N1) virus infection</b>	<ul style="list-style-type: none"> <li>• Lack of residence in/travel history to an area with ongoing transmission, or lack of close contact with a suspected/confirmed case of COVID-19 in the 14 days prior to symptom onset.</li> <li>• Close contact with infected birds (e.g., farmer or visitor to a live market in endemic areas), or living in an area when avian influenza is endemic.</li> </ul>	<ul style="list-style-type: none"> <li>• RT-PCR: positive for H5N1 viral RNA.</li> </ul>
<b>Pulmonary tuberculosis</b>	<ul style="list-style-type: none"> <li>• Consider diagnosis in endemic areas, especially</li> </ul>	<ul style="list-style-type: none"> <li>• Chest x-ray: fibronodular opacities in upper lobes with or without cavitation; atypical</li> </ul>

Condition	Differentiating signs / Differentiating tests symptoms	
	in patients who are immunocompromised. <ul style="list-style-type: none"> <li>History of symptoms is usually longer.</li> <li>Presence of night sweats and weight loss may help to differentiate.</li> </ul>	pattern includes opacities in middle or lower lobes, or hilar or paratracheal lymphadenopathy, and/or pleural effusion. <ul style="list-style-type: none"> <li>Sputum acid-fast bacilli smear and sputum culture: positive.</li> <li>Molecular testing: positive for <i>Mycoplasma tuberculosis</i>.</li> </ul>
<b>Febrile neutropenia</b>	<ul style="list-style-type: none"> <li>Suspect neutropenic sepsis in patients with a history of recent systemic anticancer treatment who present with fever (with or without respiratory symptoms) as this can be rapid and life-threatening.[477]</li> <li>Symptoms of COVID-19 and neutropenic sepsis may be difficult to differentiate at initial presentation.</li> </ul>	<ul style="list-style-type: none"> <li>CBC: neutropenia.</li> <li>RT-PCR: negative for SARS-CoV-2 viral RNA.</li> </ul>

## Diagnostic criteria

### Case definitions

Various case definitions are available:

- [WHO: public health surveillance for COVID-19 – interim guidance]
- [CDC: coronavirus disease 2019 (COVID-19) 2020 interim case definition]
- [PHE: COVID-19 – investigation and initial clinical management of possible cases]
- [ECDC: case definition for coronavirus disease 2019 (COVID-19)]



## Step-by-step treatment approach

Management predominantly depends on disease severity, and focuses on the following principles: isolation at a suitable location; infection prevention and control measures; symptom management; optimized supportive care; and organ support in severe or critical illness.

Best Practice has published a separate topic on the management of coexisting conditions in the context of COVID-19. [[BMJ Best Practice: Management of coexisting conditions in the context of COVID-19](#)]

### Key recommendations

- Consider whether the patient can be managed at home. Generally, patients with asymptomatic or mild disease can be managed at home or in a community facility.[2]
- Admit patients with moderate or severe disease to an appropriate healthcare facility. Assess adults for frailty on admission. Patients with critical disease require intensive care; involve the critical care team in discussions about admission to critical care when necessary. Monitor patients closely for signs of disease progression.[2] [495]
- Provide symptom relief as necessary. This may include treatments for fever, cough, breathlessness, anxiety, delirium, or agitation.[2] [496]
- Start supportive care according to the clinical presentation. This might include oxygen therapy, intravenous fluids, venous thromboembolism prophylaxis, high-flow nasal oxygen, noninvasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation. Sepsis and septic shock should be managed according to local protocols.[2]
- Consider empiric antibiotics if there is clinical suspicion of bacterial infection. Antibiotics may be required in patients with moderate, severe, or critical disease. Give within 1 hour of initial assessment for patients with suspected sepsis or if the patient meets high-risk criteria. Base the regimen on the clinical diagnosis, local epidemiology and susceptibility data, and local treatment guidelines.[2] [460]
- Consider systemic corticosteroid therapy for 7 to 10 days in adults with severe or critical disease. Moderate-quality evidence suggests that systemic corticosteroids probably reduce 28-day mortality in patients with severe and critical disease, and probably reduce the need for invasive ventilation.[3] [495] [497]
- Consider remdesivir in select patients with pneumonia who require supplemental oxygen. Remdesivir may reduce mortality and time to symptom resolution compared with standard of care.[3] [498] [499]
- Assess whether the patient requires any rehabilitation or follow-up after discharge. Discontinue transmission-based precautions (including isolation) and release patients from the care pathway 10 days after symptom onset plus at least 3 days without fever and respiratory symptoms.[2]
- For full details and guidance see information below.

### Location of care

The decision about location of care depends on various factors including clinical presentation, disease severity, need for supportive care, presence of risk factors for severe disease, and conditions at home (including the presence of vulnerable people). Make the decision on a case-by-case basis using the following general principles.[2]

- Mild disease: manage in a healthcare facility, in a community facility, or at home. Home isolation can be considered in most patients, including asymptomatic patients.
- Moderate disease: manage in a healthcare facility, in a community facility, or at home. Home isolation can be considered in low-risk patients (i.e., patients who are not at high risk of deterioration).
- Severe disease: manage in an appropriate healthcare facility.
- Critical disease: manage in an intensive/critical care unit.

The location of care will also depend on guidance from local health authorities and available resources. Forced quarantine orders are being used in some countries.

The strongest risk factors for hospital admission are older age (odds ratio of >2 for all age groups older than 44 years, and odds ratio of 37.9 for people ages 75 years and over), heart failure, male sex, chronic kidney disease, and increased body mass index (BMI).[500] The median time from onset of symptoms to hospital admission is around 7 days.[31] [429]

Approximately 8.6% of patients with COVID-19 who were discharged from an emergency department returned within 72 hours. Nearly 5% of patients were admitted to hospital within 72 hours of the initial visit, and 8.2% were admitted within 7 days. Risk factors associated with an increased rate of return admission included older age, abnormal chest x-ray, fever, and hypoxia on presentation.[501]

Children are less likely to require hospitalization, but if admitted, generally only require supportive care.[17] [179] Risk factors for intensive care admission in children include age <1 month, male sex, preexisting medical conditions, and presence of lower respiratory tract infection signs or symptoms at presentation.[502] The majority of children who require ventilation have underlying comorbidities, most commonly cardiac disease.[369] Children with COVID-19 are reported to have similar hospitalization rates, intensive care admission rates, and mechanical ventilator use compared with those with seasonal influenza.[471]

Overall, 19% of hospitalized patients require noninvasive ventilation, 17% require intensive care, 9% require invasive ventilation, and 2% require extracorporeal membrane oxygenation.[430] The rate of intensive care admission varies between studies; however, a meta-analysis of nearly 25,000 patients found that the admission rate was 32%, and the pooled prevalence of mortality in patients in the intensive care unit was 39%.[503] The most common reasons for intensive care unit admission are hypoxemic respiratory failure leading to mechanical ventilation and hypotension.[504] Patients admitted to intensive care units were older, were predominantly male, and had a median length of stay of 23 days (range 12 to 32 days).[505] The strongest risk factors for critical illness are oxygen saturation <88%; elevated serum troponin, C-reactive protein, and D-dimer; and, to a lesser extent, older age, BMI >40, heart failure, and male sex.[500]

## Management of mild COVID-19

Patients with suspected or confirmed mild disease (i.e., symptomatic patients meeting the case definition for COVID-19 without evidence of hypoxia or pneumonia) and asymptomatic patients should be isolated to contain virus transmission.[2]

Location of care

- Manage patients in a healthcare facility, in a community facility, or at home. Home isolation can be considered in most patients, with telemedicine or remote visits as appropriate.[2] [3] This decision

requires careful clinical judgment and should be informed by an assessment of the patient's home environment to ensure that: infection prevention and control measures and other requirements can be met (e.g., basic hygiene, adequate ventilation); the caregiver is able to provide care and recognize when the patient may be deteriorating; the caregiver has adequate support (e.g., food, supplies, psychological support); the support of a trained health worker is available in the community.[478]

#### Isolation period

- Discontinue transmission-based precautions (including isolation) and release patients from the care pathway: 10 days after positive test (asymptomatic patients); 10 days after symptom onset plus at least 3 days without fever and respiratory symptoms (symptomatic patients).[2]
- The Centers for Disease Control and Prevention (CDC) recommends discontinuing home isolation once at least 10 days have passed since symptoms first appeared, and at least 24 hours have passed since last fever without the use of antipyretics, and symptoms have improved, if a symptom-based strategy is used. In asymptomatic people, the CDC recommends discontinuing home isolation once at least 10 days have passed since the date of a positive test. Alternatively, it recommends at least two negative reverse-transcription polymerase chain reaction (RT-PCR) tests on respiratory specimens collected 24 hours apart before ending isolation if a test-based strategy is used.[506] If the patient is hospitalized, the CDC guidance for discontinuing isolation is the same as for moderate disease (see below).
- Guidance on when to stop isolation depends on local recommendations and may differ between countries. For example, in the UK the self-isolation period is 10 days in patients with milder disease who are managed in the community.[507]

#### Infection prevention and control

- For patients in home isolation, advise patients and household members to follow appropriate infection prevention and control measures:
  - [\[WHO: home care for patients with suspected or confirmed COVID-19 and management of their contacts\]](#)
  - [\[CDC: interim guidance for implementing home care of people not requiring hospitalization for coronavirus disease 2019 \(COVID-19\)\]](#)

#### Symptom management

- Fever and pain: acetaminophen or ibuprofen are recommended.[2] [496] There is no evidence at present of severe adverse events in COVID-19 patients taking nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, or of effects as a result of the use of NSAIDs on acute healthcare utilization, long-term survival, or quality of life in patients with COVID-19.[2] [496] [508] [509] [510] [511] [512] [513] Ibuprofen should only be taken at the lowest effective dose for the shortest period needed to control symptoms.
- Cough: advise patients to avoid lying on their back as this makes coughing ineffective. Use simple measures (e.g., a teaspoon of honey in patients ages 1 year and older) to help cough.[496] A meta-analysis found that honey is superior to usual care (e.g., antitussives) for the improvement of upper respiratory tract infection symptoms, particularly cough frequency and severity.[514]

- Olfactory dysfunction: consider treatment (e.g., olfactory training) if olfactory dysfunction persists beyond 2 weeks. Often it improves spontaneously and does not require specific treatment. There is no evidence to support the use of treatments in patients with COVID-19.[515]

#### Supportive care

- Advise patients about adequate nutrition and appropriate rehydration. Too much fluid can worsen oxygenation.[2]
- Advise patients to improve air circulation by opening a window or door (fans can spread infection and should not be used).[2] [496]
- Provide basic mental health and psychosocial support for all patients, and manage any symptoms of insomnia, depression, or anxiety as appropriate.[2]

#### Monitor

- Closely monitor patients with risk factors for severe illness, and counsel patients about signs and symptoms of deterioration or complications that require prompt urgent care (e.g., difficulty breathing, chest pain).[2] [3]

## Management of moderate COVID-19

Patients with suspected or confirmed moderate disease (i.e., clinical signs of pneumonia but no signs of severe pneumonia) should be isolated to contain virus transmission.[2]

#### Location of care

- Manage patients in a healthcare facility, in a community facility, or at home. Home isolation, with telemedicine or remote visits as appropriate, can be considered in low-risk patients. Manage patients at high risk of deterioration in a healthcare facility.[2] [3]

#### Isolation period

- Discontinue transmission-based precautions (including isolation) and release patients from the care pathway 10 days after symptom onset plus at least 3 days without fever and respiratory symptoms.[2]
- The CDC recommends discontinuing isolation once at least 10 days (not severely immunocompromised) or 20 days (severely immunocompromised) have passed since symptoms first appeared, and at least 24 hours have passed since last fever without the use of antipyretics, and symptoms have improved, if a symptom-based strategy is used. In asymptomatic people, the CDC recommends discontinuing home isolation once at least 10 days (not severely immunocompromised) or 20 days (severely immunocompromised) have passed since the date of a positive test. Alternatively, it recommends at least two negative RT-PCR tests on respiratory specimens collected 24 hours apart before ending isolation if a test-based strategy is used. A symptom-based strategy is preferred in these patients.[516] If the patient is isolated at home, the CDC guidance for discontinuing isolation is the same as for mild disease (see above).
- Guidance on when to stop isolation depends on local recommendations and may differ between countries. For example, in the UK the isolation period is 14 days from a positive test in hospitalized patients, and 10 days in patients with milder disease who are managed in the community.[507]

#### Infection prevention and control

- Implement local infection prevention and control procedures when managing patients with COVID-19. For patients in home isolation, advise patients and household members to follow appropriate infection prevention and control measures (see above).

#### Symptom management and supportive care

- Manage symptoms and provide supportive care as appropriate (see above).

#### Antibiotics

- Consider empiric antibiotics if there is clinical suspicion of bacterial infection.<sup>[2]</sup> <sup>[3]</sup> Antibiotics may also be considered in older people (particularly those in long-term care facilities) and children <5 years of age to provide empiric antibiotic treatment for possible pneumonia.<sup>[2]</sup>

#### Monitor

- Closely monitor patients for signs or symptoms of disease progression.
- If the patient is being managed at home, counsel them about signs and symptoms of deterioration or complications that require prompt urgent care (e.g., difficulty breathing, chest pain). There is no evidence to support the use of pulse oximeters in the home setting.<sup>[2]</sup>
- If the patient is being managed in hospital, monitor patients closely for signs of clinical deterioration using medical early warning scores (e.g., National Early Warning Score 2 [NEWS2]), and respond immediately with appropriate supportive care interventions.<sup>[2]</sup>

## Management of severe COVID-19

Patients with suspected or confirmed severe disease are at risk of rapid clinical deterioration.<sup>[2]</sup>

- Severe disease in adults is defined as having clinical signs of pneumonia plus at least one of the following:
  - Respiratory rate >30 breaths/minute
  - Severe respiratory distress
  - SpO<sub>2</sub> <90% on room air
- Severe disease in children is defined as having clinical signs of pneumonia plus at least one of the following:
  - Central cyanosis or SpO<sub>2</sub> <90%
  - Severe respiratory distress
  - General danger sign
  - Inability to breastfeed or drink, lethargy or unconsciousness, or convulsions.

#### Location of care

- Manage patients in an appropriate healthcare facility under the guidance of a specialist team.<sup>[2]</sup>
- Assess all adults for frailty on admission to hospital, irrespective of age and COVID-19 status, using the Clinical Frailty Scale (CFS). [\[Clinical frailty scale\]](#) A large observational study found that disease outcomes were better predicted by frailty than either age or comorbidity; frailty (CFS score 5-8) was associated with earlier death and longer duration of hospital stay, and these outcomes worsened with increasing frailty after adjustment for age and comorbidity.<sup>[517]</sup>

- Involve critical care teams in discussions about admission to critical care for patients where:
  - The CFS score suggests the person is less frail (e.g., CFS <5), they are likely to benefit from critical care organ support, and the patient wants critical care treatment; or
  - The CFS score suggests the person is more frail (e.g., CFS ≥5), there is uncertainty regarding the benefit of critical care organ support, and critical care advice is needed to help the decision about treatment.
- Take into account the impact of underlying pathologies, comorbidities, and severity of acute illness.[495]

#### Isolation period

- Discontinue transmission-based precautions (including isolation) and release patients from the care pathway 10 days after symptom onset plus at least 3 days without fever and respiratory symptoms.[2]
- The CDC recommends discontinuing isolation once at least 20 days have passed since symptoms first appeared, and at least 24 hours have passed since last fever without the use of antipyretics, and symptoms have improved, if a symptom-based strategy is used. In asymptomatic people, the CDC recommends discontinuing isolation once at least 20 days have passed since the date of a positive test. Alternatively, it recommends at least two negative RT-PCR tests on respiratory specimens collected 24 hours apart before ending isolation if a test-based strategy is used. A symptom-based strategy is preferred in these patients.[516]
- Guidance on when to stop isolation depends on local recommendations and may differ between countries. For example, in the UK the isolation period is 14 days from a positive test in hospitalized patients.[507]

#### Infection prevention and control

- Implement local infection prevention and control procedures when managing patients with COVID-19.

#### Oxygen

- Start supplemental oxygen therapy immediately in any patient with emergency signs (i.e., obstructed or absent breathing, severe respiratory distress, central cyanosis, shock, coma and/or convulsions), or any patient without emergency signs and SpO<sub>2</sub> <90%. [2] [3] There is no evidence of benefit for oxygen therapy in patients with COVID-19 in the absence of hypoxemia.[518]
- Target SpO<sub>2</sub> to ≥94% during resuscitation in adults and children with emergency signs who require emergency airway management and oxygen therapy. Once the patient is stable, a target SpO<sub>2</sub> >90% in children and nonpregnant adults, and ≥92% to 95% in pregnant women is recommended. Nasal prongs or a nasal cannula are preferred in young children.[2] Some guidelines recommend that SpO<sub>2</sub> should be maintained no higher than 96%. [519]
- Some centers may recommend different SpO<sub>2</sub> targets in order to support prioritization of oxygen flow for the most severely ill patients in hospital. NHS England recommends a target of 92% to 95% (or 90% to 94% if clinically appropriate), for example.[520]
- Consider positioning techniques (e.g., high supported sitting, prone position), and airway clearance management to assist with secretion clearance in adults.[2] Oxygen delivery can be increased by using a nonbreathing mask and prone positioning.[521] Consider a trial of awake prone positioning to improve oxygenation in patients with persistent hypoxemia despite increasing

supplemental oxygen requirements in whom endotracheal intubation is not otherwise indicated.[3] Early self-proning of awake, nonintubated patients has been shown to improve oxygen saturation and may delay or reduce the need for intensive care.[522] [523] [524] [525] [526]

- Monitor patients closely for signs of progressive acute hypoxemic respiratory failure. Patients who continue to deteriorate despite standard oxygen therapy require advanced oxygen/ventilatory support.[2] [3]

#### Symptom management and supportive care

- Fluids and electrolytes: use cautious fluid management in adults and children without tissue hypoperfusion and fluid responsiveness as aggressive fluid resuscitation may worsen oxygenation.[2] Correct any electrolyte or metabolic abnormalities, such as hyperglycemia or metabolic acidosis, according to local protocols.[527]
- Fever and pain: acetaminophen or ibuprofen are recommended.[2] [496] There is no evidence at present of severe adverse events in COVID-19 patients taking nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, or of effects as a result of the use of NSAIDs on acute healthcare utilization, long-term survival, or quality of life in patients with COVID-19.[508] [509] [510] [511] [512] [513] Ibuprofen should only be taken at the lowest effective dose for the shortest period needed to control symptoms.
- Cough: advise patients to avoid lying on their back as this makes coughing ineffective. Use simple measures (e.g., a teaspoon of honey in patients ages 1 year and older) to help cough. Short-term use of a cough suppressant may be considered in select patients (e.g., if the cough is distressing to the patient) provided there are no contraindications.[496] A meta-analysis found that honey is superior to usual care (e.g., antitussives) for the improvement of upper respiratory tract infection symptoms, particularly cough frequency and severity.[514]
- Breathlessness: keep the room cool, and encourage relaxation, breathing techniques, and changing body positions. Identify and treat any reversible causes of breathlessness (e.g., pulmonary edema). Consider a trial of oxygen, if available. Consider an opioid and benzodiazepine combination in patients with moderate to severe breathlessness or patients who are distressed.[496]
- Anxiety, delirium, and agitation: identify and treat any underlying or reversible causes (e.g., offer reassurance, treat hypoxia, correct metabolic or endocrine abnormalities, address coinfections, minimize use of drugs that may cause or worsen delirium, treat substance withdrawal, maintain normal sleep cycles, treat pain or breathlessness).[2] [496] Consider a benzodiazepine for the management of anxiety or agitation that does not respond to other measures. Consider haloperidol or a phenothiazine for the management of delirium.[496] Low doses of haloperidol (or another suitable antipsychotic) can also be considered for agitation.[2] Nonpharmacologic interventions are the mainstay for the management of delirium when possible, and prevention is key.[528]
- Mouth care: an important part of overall patient care in hospitalized patients who are ventilated or nonventilated and those undergoing step-down or end-of-life care.[529]
- Provide basic mental health and psychosocial support for all patients, and manage any symptoms of insomnia or depression as appropriate.[2]

#### Venous thromboembolism prophylaxis

- Start venous thromboembolism (VTE) prophylaxis in acutely ill hospitalized adults and adolescents with COVID-19 as per the standard of care for other hospitalized patients without COVID-19, provided there are no contraindications. A COVID-19 diagnosis should not influence a pediatrician's

recommendations about VTE prophylaxis in hospitalized children. Pregnant women should be managed by a specialist.[2] [3] [530] [531]

- Low molecular weight heparin or fondaparinux are preferred over unfractionated heparin in order to reduce patient contact. Unfractionated heparin is contraindicated in patients with severe thrombocytopenia. Fondaparinux is recommended in patients with a history of heparin-induced thrombocytopenia. Direct oral anticoagulants are not recommended. Mechanical thromboprophylaxis (e.g., intermittent pneumatic compression devices) is recommended if anticoagulation is contraindicated or not available.[2] [531] [532]
- The optimal dose is unknown. Standard prophylaxis doses are recommended over intermediate- or full treatment-dose regimens.[531] Some clinicians are using intermediate- or full treatment-dose regimens rather than prophylactic doses as they are worried about undetected thrombi; however, this may lead to major bleeding events.[533] There are insufficient data to recommend increased anticoagulant doses for VTE prophylaxis in COVID-19 patients outside the setting of a clinical trial.[3] However, some guidelines recommend that escalated doses can be considered in critically ill patients.[530]
- Monitor patients for signs and symptoms suggestive of thromboembolism and proceed with appropriate diagnostic and management pathways if clinically suspected.[2]
- Routine post-discharge VTE prophylaxis is not generally recommended, except in certain high-risk patients.[3] [530] [531]
- A retrospective analysis of over 4000 patients found that anticoagulation was associated with lower mortality and intubation among hospitalized COVID-19 patients. Therapeutic anticoagulation was associated with lower mortality compared with prophylactic anticoagulation, but the difference was not statistically significant.[534] However, there is little high-quality evidence for VTE prophylaxis in COVID-19 patients; therefore, clinicians should rely on pre-COVID-19 evidence-based principles of anticoagulation management combined with rational approaches to address clinical challenges.[530]

#### Antimicrobials

- Consider empiric antibiotics if there is clinical suspicion of bacterial infection. Give within 1 hour of initial assessment for patients with suspected sepsis or if the patient meets high-risk criteria (or within 4 hours of establishing a diagnosis of pneumonia); do not wait for microbiology results. Base the regimen on the clinical diagnosis (e.g., community-acquired pneumonia, hospital-acquired pneumonia, sepsis), local epidemiology and susceptibility data, and local treatment guidelines.[2] [3] [460]
- Some guidelines recommend empiric antibiotics for bacterial pathogens in all patients with community-acquired pneumonia without confirmed COVID-19. It is likely that the bacterial pathogens in patients with COVID-19 and pneumonia are the same as in previous patients with community-acquired pneumonia, and therefore empiric antimicrobial recommendations should be the same.[461] However, the National Institute for Health and Care Excellence in the UK recommends that it is reasonable not to start empiric antimicrobials if you are confident that the clinical features are typical for COVID-19.[460] There is insufficient evidence to recommend empiric broad-spectrum antimicrobials in the absence of another indication.[3]
- Some patients may require continued antibiotic therapy once COVID-19 has been confirmed depending on the clinical circumstances (e.g., clinical or microbiologic evidence of bacterial infection regardless of severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2] test results, SARS-CoV-2 test result is positive but clinical features are not typical for COVID-19). In these circumstances, review antibiotic choice based on microbiology results and switch to a

narrower-spectrum antibiotic if appropriate, review intravenous antibiotic use within 48 hours and consider switching to oral therapy, and give for a total of 5 days unless there is a clear indication to continue.[460]

- Reassess antibiotic use daily. De-escalate empiric therapy on the basis of microbiology results and clinical judgment. Regularly review the possibility of switching from intravenous to oral therapy. Duration of treatment should be as short as possible (e.g., 5 to 7 days). Antibiotic stewardship programs should be in place.[2]
- Treat laboratory-confirmed coinfections (e.g., malaria, tuberculosis, influenza) as appropriate according to local protocols.[2]

#### Corticosteroids

- The World Health Organization (WHO) strongly recommends systemic corticosteroid therapy (low-dose intravenous or oral dexamethasone or hydrocortisone) for 7 to 10 days in adults with severe or critical disease. This recommendation is based on two meta-analyses that pooled data from eight randomized trials (over 7000 patients), including the UK RECOVERY trial. Moderate-quality evidence suggests that systemic corticosteroids probably reduce 28-day mortality in patients with severe and critical disease. They also probably reduce the need for invasive ventilation. There is no evidence directly comparing dexamethasone and hydrocortisone. The harms of treatment in this context are considered to be minor. It is unclear whether these recommendations can be applied to children or those who are immunocompromised. The WHO does not recommend corticosteroids in patients with milder disease as they may increase the risk of mortality in these patients.[497] [498] [535] [536]
- In the UK, the National Institute for Health and Care Excellence recommends dexamethasone or hydrocortisone in patients with severe or critical COVID-19 (in line with WHO guidance). The marketing authorizations cover this indication in the UK.[495] [NICE: COVID-19 prescribing brief – corticosteroids]
- In Europe, the European Medicines Agency has endorsed the use of dexamethasone for patients with severe disease who require oxygen therapy or mechanical ventilation.[537]
- In the US, the National Institutes of Health guideline panel recommends using dexamethasone in adults with COVID-19 who are mechanically ventilated, and in patients who require supplemental oxygen but who are not mechanically ventilated. The panel recommends against using dexamethasone in patients who do not require supplemental oxygen. Alternative corticosteroids may be used in situations where dexamethasone is not available. Assess whether the patient is suitable for corticosteroid therapy before starting therapy.[3] The Infectious Diseases Society of America supports the use of dexamethasone in hospitalized patients with severe disease.[499]
- Monitor patients for adverse effects (e.g., hyperglycemia, secondary infections, psychiatric effects, reactivation of latent infections) and assess for drug-drug interactions.[3] Follow local policies on gastroprotection during corticosteroid treatment. Clinically significant interactions between remdesivir and corticosteroids are unlikely; however, lopinavir/ritonavir may increase hydrocortisone concentrations.[495]

#### Remdesivir

- Consider remdesivir, a broad-spectrum investigational antiviral agent, in select patients with pneumonia who require supplemental oxygen.[3] [499] Remdesivir is conditionally approved in the UK and Europe for this indication in adolescents  $\geq 12$  years of age and adults.[538] The emergency-use authorization in the US covers the treatment of suspected or confirmed COVID-19 in hospitalized children and adults, regardless of disease severity.[539]

- In the US, the National Institutes of Health recommends prioritizing remdesivir in hospitalized patients who require supplemental oxygen, but who are not on high-flow oxygen, noninvasive ventilation, mechanical ventilation, or extracorporeal membrane oxygenation (ECMO). If a patient progresses to requiring high-flow oxygen, ventilation, or ECMO while on remdesivir, the guidelines panel recommends that the course of remdesivir be completed. The panel does not recommend for or against remdesivir for the treatment of patients with severe disease who require high-flow oxygen, noninvasive ventilation, mechanical ventilation, or ECMO, or for the treatment of mild or moderate disease, as there are insufficient data for both of these groups.[3] The Infectious Diseases Society of America recommends remdesivir in hospitalized patients with severe disease who are on oxygen, mechanical ventilation, or ECMO; however, it also recommends prioritizing treatment in patients who are on oxygen therapy only when supply is limited.[499]
- Remdesivir may reduce mortality and time to symptom resolution compared with standard of care; however, there is no convincing evidence that remdesivir reduces the need for mechanical ventilation.[498] An expert guideline panel makes a weak recommendation for the use of remdesivir in severe disease, and supports more randomized trials as the quality of the evidence is low.[540]
- A UK National Institute for Health and Care Excellence review suggests there is some benefit with remdesivir compared with placebo for reducing supportive measures including mechanical ventilation and reducing time to recovery in patients who are on oxygen therapy. However, no statistically significant differences were found for mortality and serious adverse events.[541]

#### Experimental therapies

- Consider experimental therapies (e.g., convalescent plasma, lopinavir/ritonavir) only in the context of a clinical trial or according to local protocols.[2] See the Emerging section for more information.

#### Evidence for COVID-19 drug treatments

- [\[BMJ interactive tool: drug treatments for covid-19 – living systematic review and network meta-analysis\]](#)
- [\[BMJ rapid recommendations: a living WHO guideline on drugs for COVID-19\]](#)
- [\[BMJ rapid recommendations: remdesivir for severe covid-19 – a clinical practice guideline\]](#)

#### Monitor

- Monitor patients closely for signs of clinical deterioration, and respond immediately with appropriate supportive care interventions.[2]

#### Discharge and rehabilitation

- Routinely assess older patients for mobility, functional swallow, cognitive impairment, and mental health concerns, and based on that assessment determine whether the patient is ready for discharge, and whether the patient has any rehabilitation and follow-up requirements.[2]

#### Palliative care

- Palliative care interventions should be made accessible at each institution that provides care for patients with COVID-19. Identify whether the patient has an advance care plan and respect the patient's priorities and preferences when formulating the patient's care plan.[2] Follow local palliative care guidelines.

## Management of critical COVID-19

Patients with critical disease (i.e., presence of acute respiratory distress syndrome, sepsis, or septic shock) should be admitted or transferred to an intensive/critical care unit.[2]

### Location of care

- Manage patients in an intensive/critical care unit under the guidance of a specialist team.[2]
- Discuss the risks, benefits, and potential outcomes of treatment options with patients and their families, and allow them to express preferences about their management. Take their wishes and expectations into account when considering the ceiling of treatment. Use decision support tools if available. Put treatment escalation plans in place, and discuss any existing advance care plans or advance decisions to refuse treatment with patients who have preexisting advanced comorbidities.[496]

### Isolation period

- Discontinue transmission-based precautions (including isolation) and release patients from the care pathway 10 days after symptom onset plus at least 3 days without fever and respiratory symptoms.[2]
- The CDC recommends discontinuing isolation once at least 20 days have passed since symptoms first appeared, and at least 24 hours have passed since last fever without the use of antipyretics, and symptoms have improved, if a symptom-based strategy is used. In asymptomatic people, the CDC recommends discontinuing isolation once at least 20 days have passed since the date of a positive test. Alternatively, it recommends at least two negative RT-PCR tests on respiratory specimens collected 24 hours apart before ending isolation if a test-based strategy is used. A symptom-based strategy is preferred in these patients.[516]
- Guidance on when to stop isolation depends on local recommendations and may differ between countries. For example, in the UK the isolation period is 14 days from a positive test in hospitalized patients.[507]

### Infection prevention and control

- Implement local infection prevention and control procedures when managing patients with COVID-19.

### High-flow nasal oxygen or noninvasive ventilation

- Consider a trial of high-flow nasal oxygen (HFNO) or noninvasive ventilation (e.g., continuous positive airway pressure [CPAP] or bilevel positive airway pressure [BiPAP]) in selected patients with mild acute respiratory distress syndrome (ARDS).[2]
- Airborne precautions are recommended for these interventions (including bubble CPAP) due to uncertainty about the potential for aerosolization.[2] Novel methods to protect clinicians without access to standard personal protective equipment during aerosol-generating procedures have been suggested.[542] [543] [544] [545]
- Patients with hypercapnia, hemodynamic instability, multi-organ failure, or abnormal mental status should generally not receive HFNO, although emerging data suggests that it may be safe in patients with mild to moderate and nonworsening hypercapnia. Patients with hypoxemic respiratory failure and hemodynamic instability, multi-organ failure, or abnormal mental status should not receive these treatments in place of other options such as invasive ventilation.[2]

- There is ongoing debate about the optimal mode of respiratory support before mechanical ventilation.[546] NHS England recommends CPAP as the preferred form of noninvasive ventilation in patients with hypoxemic (type 1) respiratory failure. It doesn't advocate the use of HFNO based on a lack of efficacy, oxygen use (HFNO can place a strain on oxygen supplies with the risk of site supply failure), and infection spread.[547] Other guidelines recommend HFNO over noninvasive ventilation, unless HFNO is not available.[3] [519] Despite the trend to avoid HFNO, it has been shown to have a similar risk of aerosol generation to standard oxygen masks.[548]
- Early CPAP may provide a bridge to invasive mechanical ventilation. Reserve the use of BiPAP for patients with hypercapnic acute on chronic ventilatory failure (type 2 respiratory failure).[547]
- Indirect and low-certainty evidence suggests that noninvasive ventilation probably reduces mortality in patients with COVID-19, similar to mechanical ventilation, but may increase the risk of viral transmission.[549]
- Monitor patients closely for acute deterioration. If patients do not improve after a short trial of these interventions they require urgent endotracheal intubation.[2] [519]
- More detailed guidance on the management of ARDS in COVID-19 is beyond the scope of this topic; consult a specialist for further guidance.

#### Mechanical ventilation

- Consider endotracheal intubation and invasive mechanical ventilation in patients who are acutely deteriorating despite advanced oxygen/noninvasive ventilatory support measures.[2] [3]
- Two-thirds of patients who required critical care in the UK had mechanical ventilation within 24 hours of admission.[550] In New York, 33% of hospitalized patients developed respiratory failure leading to mechanical ventilation. These patients were more likely to be male, have obesity, and have elevated inflammatory markers and liver function tests.[351] Patients spent an average of 18 days on a ventilator (range 9-28 days).[551]
- Endotracheal intubation should be performed by an experienced provider using airborne precautions.[2] Intubation by video laryngoscopy is recommended if possible.[3] Young children, or adults who are obese or pregnant, may desaturate quickly during intubation and therefore require preoxygenation with 100% FiO<sub>2</sub> for 5 minutes.[2]
- Mechanically ventilated patients with ARDS should receive a lung-protective, low tidal volume/low inspiratory pressure ventilation strategy (lower targets are recommended in children). A higher positive end-expiratory pressure (PEEP) strategy is preferred over a lower PEEP strategy in moderate to severe ARDS. However, individualization of PEEP, where the patient is monitored for beneficial or harmful effects and driving pressure during titration with consideration of the risks and benefits of PEEP titration, is recommended.[2] [3] [519] NHS England recommends a low PEEP strategy in patients with normal compliance where recruitment may not be required.[552]
- Although some patients with COVID-19 pneumonia meet the criteria for ARDS, there is some discussion about whether COVID-19 pneumonia is its own specific disease with atypical phenotypes. Anecdotal evidence suggests that the main characteristic of the atypical presentation is the dissociation between well-preserved lung mechanics and the severity of hypoxemia.[553] [554] [555] [556] [557] [558] However, this approach has been criticized.[559] [560] It has been argued that an evidence-based approach extrapolating data from ARDS not related to COVID-19 is the most reasonable approach for intensive care of COVID-19 patients.[561] As a consequence of this, some clinicians have warned that protocol-driven ventilator use may be causing lung injury in some patients, and that ventilator settings should be based on physiologic findings rather than using standard protocols. High PEEP may have a detrimental effect on patients with normal compliance.[553] PEEP should always be carefully titrated.[521]

- Consider prone ventilation in patients with severe ARDS for 12 to 16 hours per day. Pregnant women in the third trimester may benefit from being placed in the lateral decubitus position. Caution is required in children.[2] [3] [519] Longer durations may be feasible in some patients.[562] A small cohort study of 12 patients in Wuhan City, China, with COVID-19-related ARDS suggests that spending periods of time in the prone position may improve lung recruitability.[563] Two small case series found that many people tolerate the prone position while awake, breathing spontaneously, or receiving noninvasive ventilation. In the patients who tolerated it, improvement in oxygenation and a decrease in respiratory rate occurred.[564] [565]
- Lung recruitment maneuvers are suggested, but staircase recruitment maneuvers are not recommended.[3] [519]
- More detailed guidance on the management of ARDS in COVID-19, including sedation and the use of neuromuscular blockade during ventilation, is beyond the scope of this topic; consult a specialist for further guidance.

#### Inhaled pulmonary vasodilator

- Consider a trial of an inhaled pulmonary vasodilator in adults who have severe ARDS and hypoxemia despite optimizing ventilation. Taper off if there is no rapid improvement in oxygenation.[3] [519]

#### Extracorporeal membrane oxygenation

- Consider ECMO according to availability and expertise if the above methods fail.[2] [519] [566] [567] ECMO is not suitable for all patients, and only those who meet certain inclusion criteria may be considered for ECMO.[568]
- There is insufficient evidence to recommend either for or against the routine use of ECMO.[3] Preliminary data on the use of ECMO in patients with COVID-19 was not promising.[569] [570] However, more recent data indicate that the estimated 60-day survival rate of ECMO-rescued patients with COVID-19 (31%) was similar to that of previous studies of ECMO for severe ARDS.[571]
- Single-access, dual-stage venovenous ECMO with early extubation appears to be safe and effective in patients with COVID-19 respiratory failure.[572]

#### Management of septic shock/sepsis

- The management of sepsis and septic shock in patients with COVID-19 is beyond the scope of this topic. See the Complications section.

#### Symptom management and supportive care

- Consider fluid and electrolyte management, antimicrobial treatment, and symptom management as appropriate (see above).
- VTE prophylaxis is recommended in critically ill patients. Low molecular weight heparin is the preferred option, with unfractionated heparin considered a suitable alternative and preferred over fondaparinux.[531]

#### Corticosteroids

- Consider systemic corticosteroids for the management of critically ill patients with COVID-19 (see above).

#### Remdesivir

- Consider remdesivir in select patients with pneumonia who require supplemental oxygen (see above).

#### Experimental therapies

- Consider experimental therapies (see the Emerging section).

#### Discharge and rehabilitation

- Routinely assess intensive care patients for mobility, functional swallow, cognitive impairment, and mental health concerns, and based on that assessment determine whether the patient is ready for discharge, and whether the patient has any rehabilitation and follow-up requirements.[2]

#### Palliative care

- Palliative care interventions should be made accessible at each institution that provides care for patients with COVID-19. Identify whether the patient has an advance care plan and respect the patient's priorities and preferences when formulating the patient's care plan.[2] Follow local palliative care guidelines.

## Management of pregnant women

Pregnant women should be managed by a multidisciplinary team, including obstetric, perinatal, neonatal, and intensive care specialists, as well as midwifery and mental health and psychosocial support. A woman-centered, respectful, skilled approach to care is recommended.[2] In women with severe or critical disease, the multidisciplinary team should be organized as soon as possible after maternal hypoxemia occurs in order to assess fetal maturity, disease progression, and the best options for delivery.[573]

There are limited data available on the management of pregnant women with COVID-19; however, pregnant women can generally be treated with the same supportive therapies detailed above, taking into account the physiologic changes that occur with pregnancy.[2]

The prevalence of asymptomatic SARS-CoV-2-positive pregnant women admitted for delivery appears to be low (<3% in a cohort in Connecticut, and 0.43% in a cohort in California).[574] [575] Screening women and their delivery partners before admission may not be helpful. More than 15% of asymptomatic maternity patients tested positive for SARS-CoV-2 infection despite having been screened negative using a telephone screening tool in one small observational study in New York. In addition to this, 58% of their asymptomatic support persons tested positive despite being screened negative.[576] Another study in a New York obstetric population found that 88% of women who tested positive for SARS-CoV-2 at admission were asymptomatic at presentation.[577]

#### Location of care

- Manage pregnant women in a healthcare facility, in a community facility, or at home. Women with suspected or confirmed mild disease may not require acute care in a hospital unless there is concern for rapid deterioration or an inability to return to hospital promptly.[2] Follow local infection prevention and control procedures as for nonpregnant people.
- Consider home care in women with asymptomatic or mild illness, provided the patient has no signs of potentially severe illness (e.g., breathlessness, hemoptysis, new chest pain/pressure, anorexia, dehydration, confusion), no comorbidities, and no obstetric issues; the patient is able to care for

herself; and monitoring and follow-up is possible. Otherwise, manage pregnant women in a hospital setting with appropriate maternal and fetal monitoring whenever possible.[408] [578] [579]

- Postpone routine prenatal or postpartum health visits for women who are in home isolation and reschedule them after the isolation period is completed. Delivery of counseling and care should be conducted via telemedicine whenever possible. Counsel women about healthy diet, mobility and exercise, intake of micronutrients, smoking, and alcohol and substance use. Advise women to seek urgent care if they develop any worsening of illness or danger signs, or danger signs of pregnancy.[2]
- The American College of Obstetricians and Gynecologists has published an algorithm to help decide whether hospital admission or home care is more appropriate. [ACOG: outpatient assessment and management for pregnant women with suspected or confirmed novel coronavirus (COVID-19)]

#### Prenatal corticosteroids

- Consider prenatal corticosteroids for fetal lung maturation in women who are at risk of preterm birth (24 to 37 weeks' gestation). Caution is advised because corticosteroids could potentially worsen the maternal clinical condition, and the decision should be made in conjunction with the multidisciplinary team.[408] [580] [579] The WHO recommends prenatal corticosteroids only when there is no clinical evidence of maternal infection and adequate childbirth and newborn care is available, and in women with mild COVID-19 after assessing the risks and benefits.[2] Corticosteroids for fetal lung maturation have not been shown to cause more harm in patients with COVID-19.[581]

#### Treatments

- Most clinical trials to date have excluded pregnant women. However, potentially effective treatments should not be withheld from pregnant women due to theoretical concerns about the safety of these therapeutic agents in pregnancy. Decisions should be made with a shared decision-making process between the patient and the clinical team.[3]
- There is no convincing evidence that systemic corticosteroids increase the incidence of congenital abnormalities. The benefits of corticosteroids in pregnant or breastfeeding women with severe or critical disease are thought to outweigh the risks.[495]

#### Labor and delivery

- Implement local infection prevention and control measures during labor and delivery. A negative pressure isolation room is recommended if available. Screen birth partners for COVID-19 infection using the standard case definition.[2]
- Individualize mode of birth based on obstetric indications and the woman's preferences. Vaginal delivery is preferred in women with confirmed infection to avoid unnecessary surgical complications. Induction of labor, interventions to accelerate labor and delivery, and cesarean delivery are generally only recommended when medically justified based on maternal and fetal condition. COVID-19 positive status alone is not an indication for cesarean section.[2] [408] [579] Avoid using birthing pools in patients with suspected or confirmed infection.[581]
- Delayed umbilical cord clamping (not earlier than 1 minute after birth) is recommended for improved maternal and infant health and nutrition outcomes. The risk of transmission via blood is thought to be minimal, and there is no evidence that delayed cord clamping increases the risk of viral transmission from the mother to the newborn.[2]

- Consider babies born to mothers with suspected or confirmed infection to be a person under investigation and isolate them from healthy newborns. Test them for infection 24 hours after birth, and, if negative, again 48 hours after birth.[582]

#### Newborn care

- Experts are divided on separating mother and baby after delivery; make decisions on a case-by-case basis using shared-decision making.
- The WHO recommends that mothers and infants should remain together unless the mother is too sick to care for her baby. Breastfeeding should be encouraged while applying appropriate infection prevention and control measures (e.g., performing hand hygiene before and after contact with the baby, wearing a mask while breastfeeding).[2] The WHO advises that the benefits of breastfeeding outweigh the potential risks for transmission.[583]
- The CDC recommends that temporary separation of a newborn from a mother with confirmed or suspected COVID-19 may be considered after weighing the risks and benefits as current evidence suggests the risk of a neonate acquiring infection from its mother is low; healthcare providers should respect maternal autonomy in the medical decision-making process. If separation is not undertaken, measures to minimize the risk of transmission should be implemented.[584] A mother with confirmed infection should be counseled to take all possible precautions to avoid transmission to the infant during breastfeeding (e.g., hand hygiene, wearing a cloth face covering). Expressed milk should be fed to the newborn by a healthy caregiver.[585]
- The Royal College of Obstetricians and Gynaecologists (RCOG) recommends that mothers with confirmed infection and healthy babies are kept together in the immediate postpartum period. It is recommended that the risks and benefits are discussed with neonatologists and families in order to individualize care in babies who may be more susceptible to infection. The RCOG advises that the benefits of breastfeeding outweigh any potential risks of transmission of the virus through breast milk, and recommends appropriate preventive precautions to limit transmission to the baby.[581]
- The American Academy of Pediatrics (AAP) recommends that temporary separation is the safest option, but acknowledges there are situations where this is not possible or the mother chooses to room-in. The AAP supports breastfeeding as the best choice for feeding. Breast milk can be expressed after appropriate hygiene measures and fed by an uninfected caregiver. If the mother chooses to breastfeed the infant themselves, appropriate prevention measures are recommended. After discharge, advise mothers with COVID-19 to practice prevention measures (e.g., distance, hand hygiene, respiratory hygiene/mask) for newborn care until either: they are afebrile for 72 hours without use of antipyretics and at least 10 days have passed since symptoms first appeared; or they have at least two consecutive negative SARS-CoV-2 tests from specimens collected  $\geq 24$  hours apart. This may require the support of an uninfected caregiver. A newborn with documented infection requires close outpatient follow-up after discharge for 14 days after birth.[582]

## Treatment details overview

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: [see disclaimer](#)

<b>Acute</b>		<b>( summary )</b>
<b>mild COVID-19</b>		
	<b>1st</b>	<b>consider home isolation</b>
	<b>plus</b>	<b>monitoring</b>
	<b>plus</b>	<b>symptom management and supportive care</b>
	<b>adjunct</b>	<b>antipyretic/analgesic</b>
<b>moderate COVID-19</b>		
	<b>1st</b>	<b>consider home isolation or hospital admission</b>
	<b>plus</b>	<b>monitoring</b>
	<b>plus</b>	<b>symptom management and supportive care</b>
	<b>adjunct</b>	<b>antibiotics</b>
	<b>adjunct</b>	<b>antipyretic/analgesic</b>
<b>severe COVID-19</b>		
	<b>1st</b>	<b>hospital admission</b>
	<b>plus</b>	<b>consider oxygen therapy</b>
	<b>plus</b>	<b>symptom management and supportive care</b>
	<b>plus</b>	<b>venous thromboembolism prophylaxis</b>
	<b>plus</b>	<b>monitoring</b>
	<b>adjunct</b>	<b>antibiotics</b>
	<b>adjunct</b>	<b>corticosteroid</b>
	<b>adjunct</b>	<b>remdesivir</b>
	<b>adjunct</b>	<b>treatment of coinfections</b>
	<b>adjunct</b>	<b>antipyretic/analgesic</b>
	<b>adjunct</b>	<b>experimental therapies</b>
	<b>adjunct</b>	<b>plan for discharge and rehabilitation</b>
	<b>adjunct</b>	<b>palliative care</b>
<b>critical COVID-19</b>		
	<b>1st</b>	<b>intensive/critical care unit admission</b>
	<b>plus</b>	<b>symptom management and supportive care</b>

**Acute****( summary )**

- plus** consider high-flow nasal oxygen or noninvasive ventilation
- plus** consider invasive mechanical ventilation
- adjunct** inhaled pulmonary vasodilator
- adjunct** extracorporeal membrane oxygenation
- adjunct** management of sepsis/septic shock
- adjunct** corticosteroid
- adjunct** remdesivir
- adjunct** experimental therapies
- adjunct** plan for discharge and rehabilitation
- adjunct** palliative care

## Treatment options

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: [see disclaimer](#)

## Acute

## mild COVID-19

**1st consider home isolation**

- » Patients with suspected or confirmed mild disease (i.e., symptomatic patients meeting the case definition for COVID-19 without evidence of hypoxia or pneumonia) and asymptomatic patients should be isolated to contain virus transmission.[2]
- » Manage patients in a healthcare facility, in a community facility, or at home. Home isolation can be considered in most patients, with telemedicine or remote visits as appropriate.[2] [3] This decision requires careful clinical judgment and should be informed by an assessment of the patient's home environment to ensure that: infection prevention and control measures and other requirements can be met (e.g., basic hygiene, adequate ventilation); the caregiver is able to provide care and recognize when the patient may be deteriorating; the caregiver has adequate support (e.g., food, supplies, psychological support); the support of a trained health worker is available in the community.[478] The location of care will depend on guidance from local health authorities and available resources.
- » Pregnant women with suspected or confirmed mild disease may not require acute care in a hospital unless there is concern for rapid deterioration or an inability to return to hospital promptly.[2]
- » Advise patients and household members to follow appropriate infection prevention and control measures:
  - » [WHO: home care for patients with suspected or confirmed COVID-19 and management of their contacts]
  - » [CDC: interim guidance for implementing home care of people not requiring hospitalization for coronavirus disease 2019 (COVID-19)]
- » Discontinue transmission-based precautions (including isolation) and release patients from the care pathway: 10 days after positive test (asymptomatic patients); 10 days after symptom onset plus at least 3 days without fever and respiratory symptoms (symptomatic patients).[2] The Centers for Disease Control and Prevention (CDC) recommends discontinuing home isolation once at least 10 days have passed since symptoms first

## Acute

appeared, and at least 24 hours have passed since last fever without the use of antipyretics, and symptoms have improved, if a symptom-based strategy is used. In asymptomatic people, the CDC recommends discontinuing home isolation once at least 10 days have passed since the date of a positive test. Alternatively, it recommends at least two negative reverse-transcription polymerase chain reaction (RT-PCR) tests on respiratory specimens collected 24 hours apart before ending isolation if a test-based strategy is used.[506] If the patient is hospitalized, CDC guidance for discontinuing isolation is the same as for moderate disease (see below). Guidance on when to stop isolation depends on local recommendations and may differ between countries. For example, in the UK the isolation period is 10 days in patients with milder disease who are managed in the community.[507]

**plus monitoring**

Treatment recommended for ALL patients in selected patient group

» Closely monitor patients with risk factors for severe illness and counsel patients about signs and symptoms of deterioration or complications that require prompt urgent care (e.g., difficulty breathing, chest pain).[2] [3]

**plus symptom management and supportive care**

Treatment recommended for ALL patients in selected patient group

» Advise patients to avoid lying on their back as this makes coughing ineffective. Use simple measures (e.g., a teaspoon of honey in patients ages 1 year and older) to help cough.[496] A meta-analysis found that honey is superior to usual care (e.g., antitussives) for the improvement of upper respiratory tract infection symptoms, particularly cough frequency and severity.[514]

» Advise patients about adequate nutrition and appropriate rehydration. Too much fluid can worsen oxygenation.[2]

» Advise patients to improve air circulation by opening a window or door (fans can spread infection and should not be used).[496]

» Provide basic mental health and psychosocial support for all patients, and manage any symptoms of insomnia, depression, or anxiety as appropriate.[2]

## Acute

» Consider treatment for olfactory dysfunction (e.g., olfactory training) if it persists beyond 2 weeks. There is no evidence to support the use of these treatments in patients with COVID-19.[515]

**adjunct antipyretic/analgesic**

Treatment recommended for SOME patients in selected patient group

**Primary options**

» **acetaminophen**: children: 10-15 mg/kg orally every 4-6 hours when required, maximum 75 mg/kg/day; adults: 325-1000 mg orally (immediate-release) every 4-6 hours when required, maximum 4000 mg/day

**OR**

» **ibuprofen**: children 6 months to 11 years of age: 5-10 mg/kg orally every 6-8 hours when required, maximum 40 mg/kg/day; children ≥12 years of age and adults: 200-400 mg orally every 4-6 hours when required, maximum 2400 mg/day

» Acetaminophen or ibuprofen are recommended.[2] [496] There is no evidence at present of severe adverse events in COVID-19 patients taking nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, or of effects as a result of the use of NSAIDs on acute healthcare utilization, long-term survival, or quality of life in patients with COVID-19.[508] [509] [510] [511] [512] [513]

» Ibuprofen should only be taken at the lowest effective dose for the shortest period needed to control symptoms. It is not recommended in pregnant women (especially in the third trimester) or children <6 months of age (age cut-offs vary by country).

## moderate COVID-19

**1st consider home isolation or hospital admission**

» Patients with suspected or confirmed moderate disease (i.e., clinical signs of pneumonia but no signs of severe pneumonia) should be isolated to contain virus transmission.[2]

» Manage patients in a healthcare facility, in a community facility, or at home. Home isolation, with telemedicine or remote visits as appropriate, can be considered in low-risk patients. Manage

## Acute

patients at high risk of deterioration and pregnant women in a healthcare facility.[2] [3]

» Implement local infection prevention and control procedures when managing patients with COVID-19. For patients in home isolation, advise patients and household members to follow appropriate infection prevention and control measures:

» [WHO: home care for patients with suspected or confirmed COVID-19 and management of their contacts]

» [CDC: interim guidance for implementing home care of people not requiring hospitalization for coronavirus disease 2019 (COVID-19)]

» Discontinue transmission-based precautions (including isolation) and release patients from the care pathway 10 days after symptom onset plus at least 3 days without fever and respiratory symptoms.[2] The Centers for Disease Control and Prevention (CDC) recommends discontinuing isolation once at least 10 days (not severely immunocompromised) or 20 days (severely immunocompromised) have passed since symptoms first appeared, and at least 24 hours have passed since last fever without the use of antipyretics, and symptoms have improved, if a symptom-based strategy is used. In asymptomatic people, the CDC recommends discontinuing isolation once at least 10 days (not severely immunocompromised) or 20 days (severely immunocompromised) have passed since the date of a positive test. Alternatively, it recommends at least two negative reverse-transcription polymerase chain reaction (RT-PCR) tests on respiratory specimens collected 24 hours apart before ending isolation if a test-based strategy is used. A symptom-based strategy is preferred in these patients.[516] If the patient is isolated at home, CDC guidance for discontinuing isolation is the same as for mild disease (see above). Guidance on when to stop isolation depends on local recommendations and may differ between countries. For example, in the UK the isolation period is 14 days from a positive test in hospitalized patients, and 10 days in patients with milder disease who are managed in the community.[507]

**plus monitoring**

Treatment recommended for ALL patients in selected patient group

» Closely monitor patients for signs or symptoms of disease progression. If the patient is being

## Acute

managed at home, counsel them about signs and symptoms of deterioration or complications that require prompt urgent care (e.g., difficulty breathing, chest pain). If the patient is being managed in hospital, monitor patients closely for signs of clinical deterioration using medical early warning scores (e.g., National Early Warning Score 2 [NEWS2]), and respond immediately with appropriate supportive care interventions.[2]

**plus symptom management and supportive care**

Treatment recommended for ALL patients in selected patient group

» Advise patients to avoid lying on their back as this makes coughing ineffective. Use simple measures (e.g., a teaspoon of honey in patients ages 1 year and older) to help cough.[496] A meta-analysis found that honey is superior to usual care (e.g., antitussives) for the improvement of upper respiratory tract infection symptoms, particularly cough frequency and severity.[514]

» Advise patients about adequate nutrition and appropriate rehydration. Too much fluid can worsen oxygenation.[2]

» Advise patients to improve air circulation by opening a window or door (fans can spread infection and should not be used).[496]

» Provide basic mental health and psychosocial support for all patients, and manage any symptoms of insomnia, depression, or anxiety as appropriate.[2]

» Consider treatment for olfactory dysfunction (e.g., olfactory training) if it persists beyond 2 weeks. There is no evidence to support the use of these treatments in patients with COVID-19.[515]

**adjunct antibiotics**

Treatment recommended for SOME patients in selected patient group

» Consider empiric antibiotics if there is clinical suspicion of bacterial infection.[2] [3] Antibiotics may also be considered in older people (particularly those in long-term care facilities) and children <5 years of age to provide empiric antibiotic treatment for possible pneumonia. The regimen should be based on the clinical diagnosis, local epidemiology and susceptibility data, and local treatment guidelines.[2]

**adjunct antipyretic/analgesic**

## Acute

Treatment recommended for SOME patients in selected patient group

### Primary options

» **acetaminophen**: children: 10-15 mg/kg orally every 4-6 hours when required, maximum 75 mg/kg/day; adults: 325-1000 mg orally (immediate-release) every 4-6 hours when required, maximum 4000 mg/day

### OR

» **ibuprofen**: children 6 months to 11 years of age: 5-10 mg/kg orally every 6-8 hours when required, maximum 40 mg/kg/day; children ≥12 years of age and adults: 200-400 mg orally every 4-6 hours when required, maximum 2400 mg/day

» Acetaminophen or ibuprofen are recommended.[2] [496] There is no evidence at present of severe adverse events in COVID-19 patients taking nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, or of effects as a result of the use of NSAIDs on acute healthcare utilization, long-term survival, or quality of life in patients with COVID-19.[508] [509] [510] [511] [512] [513]

» Ibuprofen should only be taken at the lowest effective dose for the shortest period needed to control symptoms. It is not recommended in pregnant women (especially in the third trimester) or children <6 months of age (age cut-offs vary by country).

## severe COVID-19

### 1st hospital admission

» Patients with suspected or confirmed severe disease are at risk of rapid clinical deterioration and should be admitted to an appropriate healthcare facility under the guidance of a specialist team. Severe disease in adults is defined as having clinical signs of pneumonia plus at least one of the following: respiratory rate >30 breaths/minute, severe respiratory distress, or SpO<sub>2</sub> <90% on room air. Severe disease in children is defined as having clinical signs of pneumonia plus at least one of the following: central cyanosis or SpO<sub>2</sub> <90%, severe respiratory distress, general danger sign, inability to breastfeed or drink, lethargy or unconsciousness, or convulsions).[2]

## Acute

- » Assess all adults for frailty on admission to hospital, irrespective of age and COVID-19 status, using the Clinical Frailty Scale (CFS). [\[Clinical frailty scale\]](#) Involve critical care teams in discussions about admission to critical care.[\[495\]](#) A large observational study found that disease outcomes were better predicted by frailty than either age or comorbidity; frailty (CFS score 5-8) was associated with earlier death and longer duration of hospital stay, and these outcomes worsened with increasing frailty after adjustment for age and comorbidity.[\[517\]](#)
- » Implement local infection prevention and control procedures when managing patients with COVID-19.
- » Pregnant women should be managed by a multidisciplinary team, including obstetric, perinatal, neonatal, and intensive care specialists, as well as midwifery and mental health and psychosocial support. A woman-centered, respectful, skilled approach to care is recommended.[\[2\]](#) The multidisciplinary team should be organized as soon as possible after maternal hypoxemia occurs in order to assess fetal maturity, disease progression, and the best options for delivery.[\[573\]](#)
- » Discontinue transmission-based precautions (including isolation) and release patients from the care pathway 10 days after symptom onset plus at least 3 days without fever and respiratory symptoms.[\[2\]](#) The Centers for Disease Control and Prevention (CDC) recommends discontinuing isolation once at least 20 days have passed since symptoms first appeared, and at least 24 hours have passed since last fever without the use of antipyretics, and symptoms have improved, if a symptom-based strategy is used. In asymptomatic people, the CDC recommends discontinuing isolation once at least 20 days have passed since the date of a positive test. Alternatively, it recommends at least two negative reverse-transcription polymerase chain reaction (RT-PCR) tests on respiratory specimens collected 24 hours apart before ending isolation if a test-based strategy is used. A symptom-based strategy is preferred in these patients.[\[516\]](#) Guidance on when to stop isolation depends on local recommendations and may differ between countries. For example, in the UK the isolation period is 14 days from a positive test in hospitalized patients.[\[507\]](#)

**plus consider oxygen therapy**

## Acute

Treatment recommended for ALL patients in selected patient group

» Start supplemental oxygen therapy immediately in any patient with emergency signs (i.e., obstructed or absent breathing, severe respiratory distress, central cyanosis, shock, coma and/or convulsions), or any patient without emergency signs and  $\text{SpO}_2 < 90\%$ .[\[2\]](#) [\[3\]](#)

» Target  $\text{SpO}_2$  to  $\geq 94\%$  during resuscitation in adults and children with emergency signs who require emergency airway management and oxygen therapy. Once the patient is stable, a target  $\text{SpO}_2 > 90\%$  in children and nonpregnant adults, and  $\geq 92\%$  to  $95\%$  in pregnant women, is recommended. Nasal prongs or a nasal cannula are preferred in young children.[\[2\]](#) Some guidelines recommend that  $\text{SpO}_2$  should be maintained no higher than  $96\%$ .[\[519\]](#)

» Some centers may recommend different  $\text{SpO}_2$  targets in order to support prioritization of oxygen flow for the most severely ill patients in hospital. NHS England recommends a target of  $92\%$  to  $95\%$  (or  $90\%$  to  $94\%$  if clinically appropriate), for example.[\[520\]](#)

» Consider positioning techniques (e.g., high supported sitting, prone position), and airway clearance management to assist with secretion clearance in adults.[\[2\]](#) Oxygen delivery can be increased by using a nonrebreathing mask and prone positioning.[\[521\]](#) Consider a trial of awake prone positioning to improve oxygenation in patients with persistent hypoxemia despite increasing supplemental oxygen requirements in whom endotracheal intubation is not otherwise indicated.[\[3\]](#) Early self-proning of awake, nonintubated patients has been shown to improve oxygen saturation and may delay or reduce the need for intensive care.[\[522\]](#) [\[523\]](#) [\[524\]](#) [\[525\]](#) [\[526\]](#)

» Monitor patients closely for signs of progressive acute hypoxemic respiratory failure.[\[2\]](#) [\[3\]](#)

**plus symptom management and supportive care**

Treatment recommended for ALL patients in selected patient group

» Fluids and electrolytes: use cautious fluid management in adults and children without tissue hypoperfusion and fluid responsiveness as aggressive fluid resuscitation may worsen oxygenation.[\[2\]](#) Correct any electrolyte or

## Acute

metabolic abnormalities, such as hyperglycemia or metabolic acidosis, according to local protocols.[527]

» Cough: advise patients to avoid lying on their back as this makes coughing ineffective. Use simple measures (e.g., a teaspoon of honey in patients ages 1 year and older) to help cough. Short-term use of a cough suppressant may be considered in select patients (e.g., if the cough is distressing to the patient) provided there are no contraindications.[496] A meta-analysis found that honey is superior to usual care (e.g., antitussives) for the improvement of upper respiratory tract infection symptoms, particularly cough frequency and severity.[514]

» Breathlessness: keep the room cool, and encourage relaxation, breathing techniques, and changing body positions. Identify and treat any reversible causes of breathlessness (e.g., pulmonary edema). Consider a trial of oxygen, if available. Consider an opioid and benzodiazepine combination in patients with moderate to severe breathlessness or patients who are distressed.[496]

» Anxiety, delirium, and agitation: identify and treat any underlying or reversible causes (e.g., offer reassurance, treat hypoxia, correct metabolic or endocrine abnormalities, address coinfections, minimize use of drugs that may cause or worsen delirium, treat substance withdrawal, maintain normal sleep cycles, treat pain or breathlessness).[2] [496] Consider a benzodiazepine for the management of anxiety or agitation that does not respond to other measures. Consider haloperidol or a phenothiazine for the management of delirium.[496] Low doses of haloperidol (or another suitable antipsychotic) can also be considered for agitation.[2] Nonpharmacologic interventions are the mainstay for the management of delirium when possible, and prevention is key.[528]

» Mouth care: an important part of overall patient care in hospitalized patients who are ventilated or nonventilated and those undergoing step-down or end-of-life care.[529]

» Mental health symptoms: provide basic mental health and psychosocial support for all patients, and manage any symptoms of insomnia or depression as appropriate.[2]

**plus venous thromboembolism prophylaxis**

## Acute

Treatment recommended for ALL patients in selected patient group

### Primary options

» **enoxaparin**: consult specialist for guidance on dose

**OR**

» **dalteparin**: consult specialist for guidance on dose

**OR**

» **fondaparinux**: consult specialist for guidance on dose

### Secondary options

» **heparin**: consult specialist for guidance on dose

» Start venous thromboembolism (VTE) prophylaxis in acutely ill hospitalized adults and adolescents with COVID-19 as per the standard of care for other hospitalized patients without COVID-19, provided there are no contraindications. A COVID-19 diagnosis should not influence a pediatrician's recommendations about VTE prophylaxis in hospitalized children. Pregnant women should be managed by a specialist.<sup>[2] [3] [530] [531]</sup>

» Low molecular weight heparin or fondaparinux are preferred over unfractionated heparin in order to reduce patient contact. Unfractionated heparin is contraindicated in patients with severe thrombocytopenia. Fondaparinux is recommended in patients with a history of heparin-induced thrombocytopenia. Direct oral anticoagulants are not recommended. Mechanical thromboprophylaxis (e.g., intermittent pneumatic compression devices) is recommended if anticoagulation is contraindicated or not available.<sup>[2] [531] [532]</sup>

» The optimal dose is unknown. Standard prophylaxis doses are recommended over intermediate- or full treatment-dose regimens.<sup>[531]</sup> Some clinicians are using intermediate- or full treatment-dose regimens rather than prophylactic doses as they are worried about undetected thrombi; however, this may lead to major bleeding events.<sup>[533]</sup> There are insufficient data to recommend increased anticoagulant doses for VTE prophylaxis in

## Acute

COVID-19 patients outside the setting of a clinical trial.[3] However, some guidelines recommend that escalated doses can be considered in critically ill patients.[530]

» Monitor patients for signs and symptoms suggestive of thromboembolism and proceed with appropriate diagnostic and management pathways if clinically suspected.[2]

» Routine post-discharge VTE prophylaxis is not generally recommended, except in certain high-risk patients.[3] [530] [531]

» A retrospective analysis of over 4000 patients found that anticoagulation was associated with lower mortality and intubation among hospitalized COVID-19 patients. Therapeutic anticoagulation was associated with lower mortality compared with prophylactic anticoagulation, but the difference was not statistically significant.[534] However, there is little high-quality evidence for VTE prophylaxis in COVID-19 patients; therefore, clinicians should rely on pre-COVID-19 evidence-based principles of anticoagulation management combined with rational approaches to address clinical challenges.[530]

**plus monitoring**

Treatment recommended for ALL patients in selected patient group

» Monitor patients closely for signs of clinical deterioration, and respond immediately with appropriate supportive care interventions.[2]

**adjunct antibiotics**

Treatment recommended for SOME patients in selected patient group

» Consider empiric antibiotics if there is clinical suspicion of bacterial infection. Give within 1 hour of initial assessment for patients with suspected sepsis or if the patient meets high-risk criteria (or within 4 hours of establishing a diagnosis of pneumonia); do not wait for microbiology results. Base the regimen on the clinical diagnosis (e.g., community-acquired pneumonia, hospital-acquired pneumonia, sepsis), local epidemiology and susceptibility data, and local treatment guidelines.[2] [3] [460]

» Some guidelines recommend empiric antibiotics for bacterial pathogens in all patients with community-acquired pneumonia without confirmed COVID-19. It is likely that the bacterial pathogens in patients with COVID-19 and

## Acute

pneumonia are the same as in previous patients with community-acquired pneumonia, and therefore empiric antimicrobial recommendations should be the same.[461] However, the National Institute for Health and Care Excellence in the UK recommends that it is reasonable not to start empiric antimicrobials if you are confident that the clinical features are typical for COVID-19.[460] There is insufficient evidence to recommend empiric broad-spectrum antimicrobials in the absence of another indication.[3]

» Some patients may require continued antibiotic therapy once COVID-19 has been confirmed depending on the clinical circumstances (e.g., clinical or microbiologic evidence of bacterial infection regardless of severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2] test results, SARS-CoV-2 test result is positive but clinical features are not typical for COVID-19). In these circumstances, review antibiotic choice based on microbiology results and switch to a narrower-spectrum antibiotic if appropriate, review intravenous antibiotic use within 48 hours and consider switching to oral therapy, and give for a total of 5 days unless there is a clear indication to continue.[460]

» Reassess antibiotic use daily. De-escalate empiric therapy on the basis of microbiology results and clinical judgment. Regularly review the possibility of switching from intravenous to oral therapy. Duration of treatment should be as short as possible (e.g., 5 to 7 days). Antibiotic stewardship programs should be in place.[2]

**adjunct corticosteroid**

Treatment recommended for SOME patients in selected patient group

**Primary options**

» **dexamethasone**: adults: 6 mg orally/intravenously once daily for 7-10 days

**OR**

» **hydrocortisone**: adults: 50 mg orally/intravenously every 8 hours for 7-10 days

**Secondary options**

» **prednisone**: adults: 40 mg/day orally given in 1-2 divided doses for 7-10 days

**OR**

## Acute

» [methylprednisolone](#): adults: 32 mg/day orally/intravenously given in 1-2 divided doses for 7-10 days

» The World Health Organization (WHO) strongly recommends systemic corticosteroid therapy (low-dose intravenous or oral dexamethasone or hydrocortisone) for 7 to 10 days in adults with severe COVID-19. This recommendation is based on two meta-analyses that pooled data from eight randomized trials (over 7000 patients), including the UK RECOVERY trial. Moderate-quality evidence suggests that systemic corticosteroids probably reduce 28-day mortality in patients with severe and critical COVID-19. They also probably reduce the need for invasive ventilation. There is no evidence directly comparing dexamethasone and hydrocortisone. The harms of treatment in this context are considered to be minor. It is unclear whether these recommendations can be applied to children or those who are immunocompromised.[\[497\]](#) [\[498\]](#) [\[535\]](#) [\[536\]](#)

» [\[BMJ rapid recommendations: a living WHO guideline on drugs for COVID-19\]](#)

» In the UK, the National Institute for Health and Care Excellence recommends dexamethasone or hydrocortisone in patients with severe COVID-19 (in line with WHO guidance). The marketing authorizations cover this indication in the UK.[\[495\]](#)

» [\[NICE: COVID-19 prescribing brief – corticosteroids\]](#)

» In Europe, the European Medicines Agency has endorsed the use of dexamethasone for patients with severe disease who require oxygen therapy or mechanical ventilation.[\[537\]](#)

» In the US, the National Institutes of Health guideline panel recommends using dexamethasone in adults with COVID-19 who are mechanically ventilated, and in patients who require supplemental oxygen but who are not mechanically ventilated. The panel recommends against using dexamethasone in patients who do not require supplemental oxygen. Alternative corticosteroids may be used in situations where dexamethasone is not available. Assess whether the patient is suitable for corticosteroid therapy before starting therapy.[\[3\]](#) The Infectious Diseases Society of America supports the use of dexamethasone in hospitalized patients with severe disease.[\[499\]](#)

## Acute

» Monitor patients for adverse effects (e.g., hyperglycemia, secondary infections, psychiatric effects, reactivation of latent infections) and assess for drug-drug interactions.[3] Follow local policies on gastroprotection during corticosteroid treatment. Clinically significant interactions between remdesivir and corticosteroids are unlikely; however, lopinavir/ritonavir may increase hydrocortisone concentrations.[495]

» Treatment should stop if the person is discharged from hospital before the 10-day course is completed.[495]

**adjunct remdesivir**

Treatment recommended for SOME patients in selected patient group

**Primary options**

» **remdesivir**: children: consult specialist for guidance on dose; adults: 200 mg intravenously on day 1, followed by 100 mg once daily for 4-9 days

The recommended treatment course is 5 days or until hospital discharge, whichever comes first. Some experts recommend a 10-day course in patients who have not shown clinical improvement after 5 days. National Institutes of Health. Coronavirus disease 2019 (COVID-19) treatment guidelines. 2020 [internet publication]. <https://covid19treatmentguidelines.nih.gov/>

» Consider remdesivir in select patients with pneumonia who require supplemental oxygen.[3] [499] Remdesivir is conditionally approved in the UK and Europe for this indication in adolescents  $\geq 12$  years of age and adults.[538] The emergency-use authorization in the US covers the treatment of suspected or confirmed COVID-19 in hospitalized children and adults, regardless of disease severity.[539]

» In the US, the National Institutes of Health recommends prioritizing remdesivir in hospitalized patients who require supplemental oxygen, but who are not on high-flow oxygen, noninvasive ventilation, mechanical ventilation, or extracorporeal membrane oxygenation.[3] The Infectious Diseases Society of America also recommends remdesivir in hospitalized patients with severe disease who are on oxygen.[499]

» Remdesivir may reduce mortality and time to symptom resolution compared with standard of care in patients with severe disease; however, there is no convincing evidence that

## Acute

remdesivir reduces the need for mechanical ventilation.[498]

» [BMJ interactive tool: drug treatments for covid-19 – living systematic review and network meta-analysis]

» An expert guideline panel makes a weak recommendation for the use of remdesivir in severe disease, and supports more randomized trials as the quality of the evidence is low.[540]

» [BMJ rapid recommendations: remdesivir for severe covid-19 – a clinical practice guideline]

» A UK National Institute for Health and Care Excellence review suggests there is some benefit with remdesivir compared with placebo for reducing supportive measures including mechanical ventilation and reducing time to recovery in patients who are on oxygen therapy. However, no statistically significant differences were found for mortality and serious adverse events.[541]

» Remdesivir can cause gastrointestinal symptoms, elevated transaminase levels, and an increase in prothrombin time. Hypersensitivity reactions have also been reported during and following administration. Remdesivir should not be used in patients with an estimated glomerular filtration rate <30 mL/minute, and it should be used with caution in patients with hepatic impairment. Safety and efficacy has not been evaluated in pregnant women, breastfeeding women, or children. Remdesivir should not be withheld from pregnant women if otherwise indicated. Remdesivir may interact with hydroxychloroquine/chloroquine, but is thought to be safe with corticosteroids.[3]

#### adjunct treatment of coinfections

Treatment recommended for SOME patients in selected patient group

» Treat laboratory-confirmed coinfections (e.g., malaria, tuberculosis, influenza) as appropriate according to local protocols.[2]

#### adjunct antipyretic/analgesic

Treatment recommended for SOME patients in selected patient group

#### Primary options

» **acetaminophen**: children: 10-15 mg/kg orally every 4-6 hours when required, maximum 75 mg/kg/day; adults: 325-1000 mg

## Acute

orally (immediate-release) every 4-6 hours when required, maximum 4000 mg/day

**OR**

» **ibuprofen**: children 6 months to 11 years of age: 5-10 mg/kg orally every 6-8 hours when required, maximum 40 mg/kg/day; children ≥12 years of age and adults: 200-400 mg orally every 4-6 hours when required, maximum 2400 mg/day

» Acetaminophen or ibuprofen are recommended.[2] [519] There is no evidence at present of severe adverse events in COVID-19 patients taking nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, or of effects as a result of the use of NSAIDs on acute healthcare utilization, long-term survival, or quality of life in patients with COVID-19.[508] [509] [510] [511] [512] [513]

» Ibuprofen should only be taken at the lowest effective dose for the shortest period needed to control symptoms. It is not recommended in pregnant women (especially in the third trimester) or children <6 months of age (age cut-offs vary by country).

**adjunct experimental therapies**

Treatment recommended for SOME patients in selected patient group

» Consider experimental therapies (e.g., convalescent plasma, lopinavir/ritonavir) only in the context of a clinical trial or according to local protocols.[2] See the Emerging section for more information.

**adjunct plan for discharge and rehabilitation**

Treatment recommended for SOME patients in selected patient group

» Routinely assess older patients for mobility, functional swallow, cognitive impairment, and mental health concerns, and based on that assessment determine whether the patient is ready for discharge, and whether the patient has any rehabilitation and follow-up requirements.[2]

**adjunct palliative care**

Treatment recommended for SOME patients in selected patient group

» Palliative care interventions should be made accessible at each institution that provides care for patients with COVID-19. Identify whether the patient has an advance care plan and respect

## Acute

the patient's priorities and preferences when formulating the patient's care plan.<sup>[2]</sup> Follow local palliative care guidelines.

## critical COVID-19

**1st intensive/critical care unit admission**

- » Patients with critical disease (i.e., presence of acute respiratory distress syndrome, sepsis, or septic shock) should be admitted or transferred to an intensive/critical care unit under the guidance of a specialist team.<sup>[2]</sup>
- » Discuss the risks, benefits, and potential outcomes of treatment options with patients and their families, and allow them to express preferences about their management. Take their wishes and expectations into account when considering the ceiling of treatment. Use decision support tools if available. Put treatment escalation plans in place, and discuss any existing advance care plans or advance decisions to refuse treatment with patients who have preexisting advanced comorbidities.<sup>[496]</sup>
- » Implement local infection prevention and control procedures when managing patients with COVID-19.
- » Pregnant women should be managed by a multidisciplinary team, including obstetric, perinatal, neonatal, and intensive care specialists, as well as midwifery and mental health and psychosocial support. A woman-centered, respectful, skilled approach to care is recommended.<sup>[2]</sup> The multidisciplinary team should be organized as soon as possible after maternal hypoxemia occurs in order to assess fetal maturity, disease progression, and the best options for delivery.<sup>[573]</sup>
- » Discontinue transmission-based precautions (including isolation) and release patients from the care pathway 10 days after symptom onset plus at least 3 days without fever and respiratory symptoms.<sup>[2]</sup> The Centers for Disease Control and Prevention (CDC) recommends discontinuing isolation once at least 20 days have passed since symptoms first appeared, and at least 24 hours have passed since last fever without the use of antipyretics, and symptoms have improved, if a symptom-based strategy is used. In asymptomatic people, the CDC recommends discontinuing isolation once at least 20 days have passed since the date of a positive test. Alternatively, it recommends at least two negative reverse-transcription

## Acute

polymerase chain reaction (RT-PCR) tests on respiratory specimens collected 24 hours apart before ending isolation if a test-based strategy is used. A symptom-based strategy is preferred in these patients.[516] Guidance on when to stop isolation depends on local recommendations and may differ between countries. For example, in the UK the isolation period is 14 days from a positive test in hospitalized patients.[507]

**plus symptom management and supportive care**

Treatment recommended for ALL patients in selected patient group

» Consider fluid and electrolyte management, antimicrobial treatment, and symptom management as appropriate. Venous thromboembolism prophylaxis is recommended in critically ill patients. Low molecular weight heparin is the preferred option, with unfractionated heparin considered a suitable alternative and preferred over fondaparinux.[531] See Severe COVID-19 above for more detailed information.

» Implement standard interventions to prevent complications associated with critical illness.[2]

**plus consider high-flow nasal oxygen or noninvasive ventilation**

Treatment recommended for ALL patients in selected patient group

» Consider a trial of high-flow nasal oxygen (HFNO) or noninvasive ventilation (e.g., continuous positive airway pressure [CPAP] or bilevel positive airway pressure [BiPAP]) in selected patients with mild acute respiratory distress syndrome.[2]

» Airborne precautions are recommended for these interventions (including bubble CPAP) due to uncertainty about the potential for aerosolization.[2]

» Patients with hypercapnia, hemodynamic instability, multi-organ failure, or abnormal mental status should generally not receive HFNO, although emerging data suggest that it may be safe in patients with mild to moderate and nonworsening hypercapnia. Patients with hypoxemic respiratory failure and hemodynamic instability, multi-organ failure, or abnormal mental status should not receive these treatments in place of other options such as invasive ventilation.[2]

## Acute

» There is ongoing debate about the optimal mode of respiratory support before mechanical ventilation.[546] NHS England recommends CPAP as the preferred form of noninvasive ventilation in patients with hypoxemic (type 1) respiratory failure. It doesn't advocate the use of HFNO based on a lack of efficacy, oxygen use (HFNO can place a strain on oxygen supplies with the risk of site supply failure), and infection spread.[547] Other guidelines recommend HFNO over noninvasive ventilation, unless HFNO is not available.[3] [519] Despite the trend to avoid HFNO, it has been shown to have a similar risk of aerosol generation to standard oxygen masks.[548]

» Early CPAP may provide a bridge to invasive mechanical ventilation. Reserve the use of BiPAP for patients with hypercapnic acute on chronic ventilatory failure (type 2 respiratory failure).[547]

» Monitor patients closely for acute deterioration. If patients do not improve after a short trial of these interventions, they require urgent endotracheal intubation.[2] [519]

**plus consider invasive mechanical ventilation**

Treatment recommended for ALL patients in selected patient group

» Consider endotracheal intubation and mechanical ventilation in patients who are acutely deteriorating despite advanced oxygen/noninvasive ventilatory support measures.[2] [3]

» Endotracheal intubation should be performed by an experienced provider using airborne precautions.[2] Intubation by video laryngoscopy is recommended if possible.[3] Young children, or adults who are obese or pregnant, may desaturate quickly during intubation and therefore require preoxygenation with 100% fraction of inspired oxygen (FiO<sub>2</sub>) for 5 minutes.[2]

» Mechanically ventilated patients with acute respiratory distress syndrome (ARDS) should receive a lung-protective, low tidal volume/low inspiratory pressure ventilation strategy (lower targets are recommended in children). A higher positive end-expiratory pressure (PEEP) strategy is preferred over a lower PEEP strategy in moderate to severe ARDS. However, individualization of PEEP, where the patient is monitored for beneficial or harmful effects and driving pressure during titration with consideration of the risks and benefits of PEEP

## Acute

titration, is recommended.[2] [3] [519] NHS England recommends a low PEEP strategy in patients with normal compliance where recruitment may not be required.[552]

» Although some patients with COVID-19 pneumonia meet the criteria for ARDS, there is some discussion about whether COVID-19 pneumonia is its own specific disease with atypical phenotypes. Anecdotal evidence suggests that the main characteristic of the atypical presentation is the dissociation between well-preserved lung mechanics and the severity of hypoxemia.[553] [554] [555] [556] [557] [558] However, this approach has been criticized.[559] [560] It has been argued that an evidence-based approach extrapolating data from ARDS not related to COVID-19 is the most reasonable approach for intensive care of COVID-19 patients.[561] As a consequence of this, some clinicians have warned that protocol-driven ventilator use may be causing lung injury in some patients, and that ventilator settings should be based on physiologic findings rather than using standard protocols. High PEEP may have a detrimental effect on patients with normal compliance.[553] PEEP should always be carefully titrated.[521]

» Consider prone ventilation in patients with severe ARDS for 12 to 16 hours per day. Pregnant women in the third trimester may benefit from being placed in the lateral decubitus position. Caution is required in children.[2] [3] [519] Longer durations may be feasible in some patients.[562]

» Lung recruitment maneuvers are suggested, but staircase recruitment maneuvers are not recommended.[3] [519]

#### adjunct **inhaled pulmonary vasodilator**

Treatment recommended for SOME patients in selected patient group

» Consider a trial of an inhaled pulmonary vasodilator in adults who have severe acute respiratory distress syndrome and hypoxemia despite optimizing ventilation. Taper off if there is no rapid improvement in oxygenation.[3] [519]

#### adjunct **extracorporeal membrane oxygenation**

Treatment recommended for SOME patients in selected patient group

» Consider extracorporeal membrane oxygenation (ECMO) according to availability and expertise if the above methods fail.[2] [519]

## Acute

[566] [567] ECMO is not suitable for all patients, and only those who meet certain inclusion criteria may be considered for ECMO.[568]

» There is insufficient evidence to recommend either for or against the routine use of ECMO.[3] Preliminary data on the use of ECMO in patients with COVID-19 was not promising.[569] [570] However, more recent data indicate that the estimated 60-day survival rate of ECMO-rescued patients with COVID-19 (31%) was similar to that of previous studies of ECMO for severe ARDS.[571]

» Single-access, dual-stage venovenous ECMO with early extubation appears to be safe and effective in patients with COVID-19 respiratory failure.[572]

#### adjunct management of sepsis/septic shock

Treatment recommended for SOME patients in selected patient group

» The management of sepsis and septic shock in patients with COVID-19 is beyond the scope of this topic. See the Complications section.

#### adjunct corticosteroid

Treatment recommended for SOME patients in selected patient group

##### Primary options

» **dexamethasone**: adults: 6 mg orally/intravenously once daily for 7-10 days

##### OR

» **hydrocortisone**: adults: 50 mg orally/intravenously every 8 hours for 7-10 days  
May be continued for up to 28 days for patients with septic shock. National Institute for Health and Care Excellence. COVID-19 rapid guideline: critical care in adults. 2020 [internet publication]. <https://www.nice.org.uk/guidance/ng159>

##### Secondary options

» **prednisone**: adults: 40 mg/day orally given in 1-2 divided doses for 7-10 days

##### OR

» **methylprednisolone**: adults: 32 mg/day orally/intravenously given in 1-2 divided doses for 7-10 days

## Acute

» The World Health Organization (WHO) strongly recommends systemic corticosteroid therapy (low-dose intravenous or oral dexamethasone or hydrocortisone) for 7 to 10 days in adults with critical COVID-19. This recommendation is based on two meta-analyses that pooled data from eight randomized trials (over 7000 patients), including the UK RECOVERY trial. Moderate-quality evidence suggests that systemic corticosteroids probably reduce 28-day mortality in patients with severe and critical COVID-19. They also probably reduce the need for invasive ventilation. There is no evidence directly comparing dexamethasone and hydrocortisone. The harms of treatment in this context are considered to be minor. It is unclear whether these recommendations can be applied to children or those who are immunocompromised.[497] [498] [535] [536]

» [BMJ rapid recommendations: a living WHO guideline on drugs for COVID-19]

» In the UK, the National Institute for Health and Care Excellence recommends dexamethasone or hydrocortisone in patients with critical COVID-19 (in line with WHO guidance). The marketing authorizations cover this indication in the UK.[495]

» [NICE: COVID-19 prescribing brief – corticosteroids]

» In Europe, the European Medicines Agency has endorsed the use of dexamethasone for patients with severe disease who require oxygen therapy or mechanical ventilation.[537]

» In the US, the National Institutes of Health guideline panel recommends using dexamethasone in adults with COVID-19 who are mechanically ventilated, and in patients who require supplemental oxygen but who are not mechanically ventilated. The panel recommends against using dexamethasone in patients who do not require supplemental oxygen. Alternative corticosteroids may be used in situations where dexamethasone is not available. Assess whether the patient is suitable for corticosteroid therapy before starting therapy.[3] The Infectious Diseases Society of America supports the use of dexamethasone in hospitalized patients with severe disease.[499]

» Monitor patients for adverse effects (e.g., hyperglycemia, secondary infections, psychiatric effects, reactivation of latent infections) and assess for drug-drug interactions.[3] Follow local

## Acute

policies on gastroprotection during corticosteroid treatment. Clinically significant interactions between remdesivir and corticosteroids are unlikely; however, lopinavir/ritonavir may increase hydrocortisone concentrations.[495]

» Treatment should stop if the person is discharged from hospital before the 10-day course is completed.[495]

**adjunct remdesivir**

Treatment recommended for SOME patients in selected patient group

**Primary options**

» **remdesivir**: children: consult specialist for guidance on dose; adults: 200 mg intravenously on day 1, followed by 100 mg once daily for 4-9 days

The recommended treatment course is 5 days or until hospital discharge, whichever comes first. Some experts recommend a 10-day course in patients who have not shown clinical improvement after 5 days. National Institutes of Health. Coronavirus disease 2019 (COVID-19) treatment guidelines. 2020 [internet publication]. <https://covid19treatmentguidelines.nih.gov/> A 10-day course is also recommend in patients on mechanical ventilation or ECMO. Bhimraj A, Morgan RL, Hirsch Shumaker A, et al. Infectious Diseases Society of America guidelines on the treatment and management of patients with COVID-19. 2020 [internet publication]. <https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/>

» Consider remdesivir in select patients with pneumonia who require supplemental oxygen.[3] [499] Remdesivir is conditionally approved in the UK and Europe for this indication in adolescents  $\geq 12$  years of age and adults.[538] The emergency-use authorization in the US covers the treatment of suspected or confirmed COVID-19 in hospitalized children and adults, regardless of disease severity.[539]

» In the US, the National Institutes of Health recommends prioritizing remdesivir in hospitalized patients who require supplemental oxygen, but who are not on high-flow oxygen, noninvasive ventilation, mechanical ventilation, or extracorporeal membrane oxygenation (ECMO). If a patient progresses to requiring high-flow oxygen, ventilation, or ECMO while on remdesivir, the guidelines panel recommends

## Acute

that the course of remdesivir be completed. The panel does not recommend for or against remdesivir for the treatment of patients who require high-flow oxygen, noninvasive ventilation, mechanical ventilation, or ECMO as there are insufficient data.<sup>[3]</sup> The Infectious Diseases Society of America recommends remdesivir in hospitalized patients with severe disease who are on oxygen, mechanical ventilation, or ECMO; however, it also recommends prioritizing treatment in patients who are on oxygen therapy only when supply is limited.<sup>[499]</sup>

» Remdesivir may reduce mortality and time to symptom resolution compared with standard of care in patients with severe disease; however, there is no convincing evidence that remdesivir reduces the need for mechanical ventilation.<sup>[498]</sup>

» [\[BMJ interactive tool: drug treatments for covid-19 – living systematic review and network meta-analysis\]](#)

» An expert guideline panel makes a weak recommendation for the use of remdesivir in severe disease, and supports more randomized trials as the quality of the evidence is low.<sup>[540]</sup>

» [\[BMJ rapid recommendations: remdesivir for severe covid-19 – a clinical practice guideline\]](#)

» A UK National Institute for Health and Care Excellence review suggests there is some benefit with remdesivir compared with placebo for reducing supportive measures including mechanical ventilation and reducing time to recovery in patients who are on oxygen therapy. However, no statistically significant differences were found for mortality and serious adverse events.<sup>[541]</sup>

» Remdesivir can cause gastrointestinal symptoms, elevated transaminase levels, and an increase in prothrombin time. Hypersensitivity reactions have also been reported during and following administration. Remdesivir should not be used in patients with an estimated glomerular filtration rate <30 mL/minute, and it should be used with caution in patients with hepatic impairment. Safety and efficacy has not been evaluated in pregnant women, breastfeeding women, or children. Remdesivir should not be withheld from pregnant women if otherwise indicated. Remdesivir may interact with hydroxychloroquine/chloroquine, but is thought to be safe with corticosteroids.<sup>[3]</sup>

## Acute

**adjunct experimental therapies**

Treatment recommended for SOME patients in selected patient group

» Consider experimental therapies (e.g., convalescent plasma, lopinavir/ritonavir) only in the context of a clinical trial or according to local protocols.[2] See the Emerging section for more information.

**adjunct plan for discharge and rehabilitation**

Treatment recommended for SOME patients in selected patient group

» Routinely assess intensive care patients for mobility, functional swallow, cognitive impairment, and mental health concerns, and based on that assessment determine whether the patient is ready for discharge, and whether the patient has any rehabilitation and follow-up requirements.[2]

**adjunct palliative care**

Treatment recommended for SOME patients in selected patient group

» Palliative care interventions should be made accessible at each institution that provides care for patients with COVID-19. Identify whether the patient has an advance care plan and respect the patient's priorities and preferences when formulating the patient's care plan.[2] Follow local palliative care guidelines.

# Emerging

## Introduction

Various treatments for COVID-19 are in clinical trials around the world. [\[Global coronavirus COVID-19 clinical trial tracker\]](#) There are several treatments being used off-label on a compassionate-use basis, or as part of a clinical trial. [\[WHO: off-label use of medicines for COVID-19\]](#) It is important to note that there may be serious adverse effects associated with these drugs, and that these adverse effects may overlap with the clinical manifestations of COVID-19. These drugs may also increase the risk of death in an older patient or a patient with an underlying health condition (e.g., drugs that prolong the QT interval may increase the risk of cardiac death).[\[586\]](#) Drug-drug interactions with the patient's existing medication(s), and drug-disease interactions (e.g., impact of inflammation on drug metabolism in COVID-19 patients), must also be considered.[\[587\]](#) International trials to identify treatments that may be beneficial, such as the World Health Organization's (WHO) Solidarity trial and the UK's randomized evaluation of COVID-19 therapy (RECOVERY) trial, are ongoing. [\[WHO: "Solidarity" clinical trial for COVID-19 treatments\]](#) [\[RECOVERY trial\]](#)

## Convalescent plasma

Clinical trials to determine the safety and efficacy of convalescent plasma that contains antibodies to SARS-CoV-2 in patients with COVID-19 are ongoing. In the US, the Food and Drug Administration has issued an emergency-use authorization for convalescent plasma for the treatment of COVID-19 in hospitalized patients.[\[588\]](#) This follows publication of a preprint (not peer reviewed) of an open-label, multicenter, expanded access program study of over 35,000 patients that found convalescent plasma lowered 7-day mortality by 9% in hospitalized patients when given within 3 days of diagnosis, and by 12% when given 4 or more days later.[\[589\]](#) A meta-analysis and systematic review with a total of 5444 patients found that the use of convalescent plasma reduced mortality, increased viral clearance, and resulted in clinical improvement in patients with COVID-19; however, the evidence is of low quality and further randomized controlled trials are required.[\[590\]](#) The authors of a Cochrane rapid review were uncertain as to whether convalescent plasma is beneficial for hospitalized patients with COVID-19. The completed studies were of poor quality, and the results could be related to natural progression of the disease or to other treatments the patient receives. The currently available evidence on the safety and efficacy of convalescent plasma for the treatment of hospitalized patients is of very low certainty.[\[591\]](#) The National Institutes of Health guidelines panel says that there is currently insufficient evidence to recommend either for or against the use of convalescent plasma for the treatment of COVID-19.[\[3\]](#) The Infectious Diseases Society of America recommends convalescent plasma only in the context of a clinical trial.[\[499\]](#)

## Hydroxychloroquine/chloroquine

Hydroxychloroquine and chloroquine are oral drugs that are indicated for the prophylaxis and treatment of malaria, as well as the treatment of some autoimmune conditions. Both drugs show in vitro activity against SARS-CoV-2; however, hydroxychloroquine has been used more commonly in trials due to its better adverse-effect profile.[\[592\]](#) [\[593\]](#) Initial data from clinical trials of hydroxychloroquine seemed promising.[\[594\]](#) [\[595\]](#) [\[596\]](#) However, a living systematic review of current evidence (as of 27 August) concludes that there is low-strength evidence from trials and cohort studies that hydroxychloroquine has no positive effect on all-cause mortality or the need for mechanical ventilation. Trials show low strength of evidence for no positive effect on intubation or death and discharge from the hospital, whereas evidence from cohort studies about these outcomes remains insufficient. Data are insufficiently strong to support a treatment benefit of hydroxychloroquine for other outcomes.[\[597\]](#) [\[598\]](#) However, hydroxychloroquine may reduce time to symptom resolution.[\[498\]](#) A meta-analysis of randomized controlled trials found that hydroxychloroquine showed no benefit in the treatment of mild to moderate disease also.[\[599\]](#) The WHO and the National Institutes of Health have prematurely discontinued their clinical trials of hydroxychloroquine citing a lack of efficacy; however, results are yet to be published. Preliminary results from the UK RECOVERY trial found that hydroxychloroquine does not reduce the risk of dying or improve other outcomes in hospitalized patients, and investigators have stopped enrolling participants into the hydroxychloroquine arm of the trial.[\[600\]](#) The National Institutes of Health guideline panel recommends against the use of hydroxychloroquine or chloroquine for the treatment of COVID-19 in hospitalized patients. The panel recommends against the use of both drugs in nonhospitalized patients except in the context of a clinical trial.[\[3\]](#) The Infectious

Diseases Society of America strongly recommends against the use of hydroxychloroquine or chloroquine (with or without azithromycin) for the treatment of COVID-19 in hospitalized patients based on moderate-quality evidence.[499] The FDA has revoked its emergency-use authorization for hydroxychloroquine and chloroquine as it believes the potential benefits no longer outweigh the known and potential risks.[531] If used, hydroxychloroquine and chloroquine should be used with caution in patients with preexisting cardiovascular disease due to the risk of arrhythmias, and a baseline echocardiogram is recommended before treatment, particularly in patients who are critically ill.[601] [602] Caution is recommended when using these drugs with other drugs that prolong the QT interval (e.g., azithromycin) due to an increased risk of QT interval prolongation and/or ventricular tachycardia (including Torsades de Pointes).[603] [604] [605]

## Lopinavir/ritonavir

An oral antiretroviral protease inhibitor currently approved for the treatment of HIV Infection. Lopinavir/ritonavir has been used in clinical trials for the treatment of COVID-19. Results from one small case series found that evidence of clinical benefit with lopinavir/ritonavir was equivocal.[606] A randomized controlled trial of 200 patients with severe disease found that treatment with lopinavir/ritonavir plus standard care (i.e., oxygen, noninvasive and invasive ventilation, antibiotics, vasopressors, renal replacement therapy, and extracorporeal membrane oxygenation, as necessary) was not associated with an decreased time to clinical improvement compared with standard care alone, and 28-day mortality was similar in both groups.[607] Preliminary results from the UK RECOVERY trial found that there is no beneficial effect of lopinavir/ritonavir in hospitalized patients with COVID-19. There was no significant difference in 28-day mortality, risk of progression to mechanical ventilation, or duration of hospital stay between the two treatment arms (lopinavir/ritonavir versus usual care alone), and the results were consistent in different subgroups of patients.[608] Interim data from the WHO Solidarity trial found that lopinavir/ritonavir has little or no reduction in the mortality of hospitalized COVID-19 patients when compared with standard of care.[609] However, lopinavir/ritonavir may reduce time to symptom resolution.[498] Lopinavir/ritonavir causes QT interval prolongation and may increase the risk of bradycardia, especially in older, critically ill patients.[610] The National Institutes of Health guidelines panel recommends against the use of lopinavir/ritonavir for the treatment of COVID-19 except in the context of a clinical trial.[3] [Centre for Evidence-Based Medicine: lopinavir/ritonavir – a rapid review of effectiveness in COVID-19]

## Intravenous immune globulin

Intravenous immune globulin (IVIg) is being trialed in some patients with COVID-19.[32] [611] A retrospective study of 58 patients with severe COVID-19 found that IVIg, when used as an adjuvant treatment within 48 hours of admission, may reduce the use of mechanical ventilation, reduce hospital/intensive care unit stay, and reduce 28-day mortality; however, this study had several limitations.[612] There is currently insufficient evidence to recommend IVIg for the treatment of COVID-19.[613] The National Institutes of Health guidelines panel recommends against the use of non-SARS-CoV-2-specific IVIg for the treatment of COVID-19 except in the context of a clinical trial.[3]

## Monoclonal antibody treatments

SARS-CoV-2 monoclonal antibodies have the potential to be used for prophylaxis and treatment of COVID-19.[614] Recombinant, fully human monoclonal neutralizing antibodies, such as JS016 and LY-COV555, are in development. These antibodies bind to the SARS-CoV-2 surface spike protein receptor binding domain, which blocks the binding of the virus to the angiotensin-converting enzyme-2 (ACE2) host cell surface receptor. Both antibody treatments have started phase 1 studies.[615] [616] Novel multi-antibody cocktail therapies (e.g., REGN-COV2) are also in clinical trials for prophylaxis or treatment.[617] The UK RECOVERY trial is investigating whether adding REGN-COV2 to usual standard of care (versus standard care alone) has any impact on all-cause 28-day mortality.[618]

## Interleukin-6 (IL-6) inhibitors

IL-6 inhibitors (e.g., tocilizumab, siltuximab) are being trialed in COVID-19 patients for the treatment of virus-induced cytokine release syndrome. These drugs are already approved in some countries for other indications. A meta-analysis of 23 observational studies found that tocilizumab plus standard of care may reduce mortality and the need for mechanical ventilation in patients with severe disease.[619] The

randomized controlled phase 3 EMPACTA trial found that tocilizumab reduced the need for mechanical ventilation in hospitalized patients compared with placebo, although there was no statistical difference in mortality between the two arms.[620] However, the randomized controlled phase 3 COVACTA trial failed to meet its primary end point of clinical status, and found that tocilizumab did not improve mortality.[621] Full results of both trials are yet to be published. The National Institutes of Health guidelines panel recommends against the use of IL-6 inhibitors for the treatment of COVID-19 except in the context of a clinical trial.[3]

## Anakinra

Anakinra, an interleukin-1 inhibitor, is being trialed in COVID-19 patients for the treatment of virus-induced cytokine release syndrome. It is already approved in some countries for other indications. Addition of high-dose intravenous anakinra to noninvasive ventilation and standard care (which included hydroxychloroquine and lopinavir/ritonavir) in COVID-19 patients with moderate to severe acute respiratory distress syndrome and hyperinflammation was associated with a higher survival rate at 21 days in a small retrospective study.[622] A small prospective cohort study found that anakinra significantly reduced the need for invasive mechanical ventilation and mortality in patients with severe disease.[623] A small retrospective case series found that anakinra could be beneficial in patients with cytokine release syndrome when initiated early after the onset of acute hypoxic respiratory failure.[624] The National Institutes of Health guidelines panel states that there is currently insufficient evidence to recommend either for or against the use of anakinra for the treatment of COVID-19.[3] The National Institute for Health and Care Excellence in the UK states that there is no evidence available to determine whether anakinra is effective, safe, or cost-effective for treating adults and children with secondary hemophagocytic lymphohistiocytosis triggered by SARS-CoV-2 or a similar coronavirus.[625]

## Antigranulocyte–macrophage colony-stimulating factor (GM-CSF) monoclonal antibodies

Mavrilimumab was associated with improved clinical outcomes compared with standard care in nonmechanically ventilated patients with severe disease and systemic hyperinflammation in a single-center prospective cohort study.[626] Lenzilumab was associated with a reduction in the relative risk of progression to invasive mechanical ventilation and/or death in high-risk COVID-19 patients with severe pneumonia compared with a matched control cohort of patients who received standard care alone in a small study of 39 patients.[627] [628]

## Janus kinase inhibitors

Janus kinase inhibitors (e.g., fedratinib, ruxolitinib, baricitinib) are currently in clinical trials for the treatment of COVID-19-associated cytokine release syndrome.[629] [630] [631] Initial data emerging from the Adaptive COVID-19 Treatment Trial indicates that baricitinib plus remdesivir reduces time to recovery in hospitalized patients compared with remdesivir alone.[632] The National Institutes of Health guidelines panel recommends against the use of Janus kinase inhibitors for the treatment of COVID-19 except in the context of a clinical trial.[3]

## Stem cell therapy

Stem cell therapy is being investigated to treat patients with COVID-19 in clinical trials. It is thought that mesenchymal stem cells can reduce the pathologic changes that occur in the lungs, and inhibit the cell-mediated immune inflammatory response.[633] The National Institutes of Health guidelines panel recommends against the use of mesenchymal stem cells for the treatment of COVID-19 except in the context of a clinical trial.[3] Adipose-derived mesenchymal stem cells have been approved by the FDA for the treatment of severe COVID-19.

## Granulocyte colony-stimulating factor (G-CSF)

Recombinant G-CSF plus usual care did not accelerate clinical improvement compared with usual care alone according to preliminary findings from a randomized clinical trial in patients with lymphopenia and no comorbidities. Larger studies are needed to determine whether G-CSF, which increases peripheral blood leukocyte and lymphocyte cell counts, is beneficial in COVID-19 patients.[634]

## Bacille Calmette-Guerin (BCG) vaccine

The BCG vaccine is being trialed in some countries for the prevention of COVID-19, including in healthcare workers. There is some evidence that BCG vaccination prevents other respiratory tract infections in children and older people mediated by induction of innate immune memory.[635] However, there is no evidence to support its use in COVID-19, and the WHO does not recommend it for the prevention of COVID-19.[636]

## Bemcentinib

An experimental small molecule that inhibits AXL kinase. Bemcentinib has previously demonstrated a role in the treatment of cancer, but has also been reported to have antiviral activity in preclinical models, including activity against SARS-CoV-2. It was the first candidate to be selected as part of the UK's Accelerating COVID-19 Research and Development (ACCORD) study.[637] The study has stopped recruiting new patients into the trial due to the reduction of new COVID-19 cases in the UK. Patients already recruited will continue on treatment as per the study protocol.

## Angiotensin-II receptor antagonists

Angiotensin-II receptor antagonists such as losartan are being investigated as a potential treatment because it is thought that the angiotensin-converting enzyme-2 (ACE2) receptor is the main binding site for the virus.[638] [639] [640] However, some experts believe that these drugs may worsen COVID-19 due to overexpression of ACE2 in people taking these drugs.

## Other antivirals

Various other antiviral drugs (monotherapy and combination therapy) are being trialed in patients with COVID-19 (e.g., oseltamivir, darunavir, ganciclovir, favipiravir, baloxavir marboxil, umifenovir, ribavirin, interferon, leronlimab).[641] [642] [643] [644] [645] [646] [647] [648] [649] [650] There is no evidence to support the use of umifenovir.[651] Triple therapy with interferon beta-1b, lopinavir/ritonavir, and ribavirin has been tested in hospitalized COVID-19 patients in a small open-label randomized phase 2 trial. Patients who received triple therapy had a significantly shorter median time to a negative nasopharyngeal swab result compared with the control group (lopinavir/ritonavir only). Patients had mild to moderate disease at the time of enrolment.[652] Clinical trials of inhaled remdesivir, and remdesivir plus interferon beta-1a, have started.[653] The National Institutes of Health guidelines panel recommends against the use of interferons for the treatment of severe or critically ill patients, except in the context of a clinical trial.[3]

## Antibiotics

The PRINCIPLE trial in the UK is currently evaluating three treatment strategies in older people (people ages over 65 years, or people ages over 50 years with an underlying health condition): usual care alone; usual care plus azithromycin; and usual care plus doxycycline.[654]

## Ivermectin

Ivermectin, a broad-spectrum antiparasitic agent, has been shown to be effective against SARS-CoV-2 in vitro.[655] It is unclear whether the doses necessary to achieve antiviral activity against SARS-CoV-2 are attainable in humans.[656] Numerous registered clinical studies of ivermectin, either alone or in combination with other drugs (e.g., doxycycline, hydroxychloroquine), are ongoing in many countries for the treatment or prevention of COVID-19. Further research in randomized controlled trials is necessary. The National Institutes of Health guidelines panel recommends against the use of ivermectin for the treatment of COVID-19 except in the context of a clinical trial.[3]

## Vitamin C

Vitamin C supplementation has shown promise in the treatment of viral infections.[657] High-dose intravenous vitamin C is being trialed in some centers for the treatment of severe COVID-19.[658] There is no evidence to support or refute the use of vitamin C in the treatment of patients with COVID-19; however, a

substantial number of trials are ongoing.[659] The National Institutes of Health guidelines panel states that there is insufficient data to recommend either for or against vitamin C.[3]

## Vitamin D

Vitamin D supplementation has been associated with a reduced risk of respiratory infections such as influenza in some studies.[660] [661] [662] Vitamin D is being trialed in patients with COVID-19.[663] [664] However, there is no evidence to recommend vitamin D for the prophylaxis or treatment of COVID-19 as yet.[665] A pilot randomized controlled trial found that high-dose calcifediol, a vitamin D3 analog, significantly reduced the need for intensive care unit treatment in hospitalized patients, and may improve clinical outcomes.[666] The UK National Institute for Health and Care Excellence states that while there is no evidence to support taking vitamin D specifically to prevent or treat COVID-19, it does recommend that all people should take a vitamin D supplement daily as per UK government advice to maintain bone and muscle health during the pandemic, especially if they are not getting enough sun exposure due to shielding or self-isolating.[667] The National Institutes of Health guidelines panel states that there is insufficient data to recommend either for or against vitamin D.[3]

## Probiotics

There is emerging evidence that gut dysbiosis may have a role in the pathogenesis of COVID-19.[292] [293] [294] Probiotics may represent a complementary approach for the prevention or treatment of mucosal damage or inflammation through the modulation of gut microbiota; however, further research is required.[668]

## Traditional Chinese medicine

Traditional Chinese medicine is being used in patients with COVID-19 in China according to local guidelines and as part of clinical trials.[669]

## Hyperbaric oxygen

Preliminary evidence suggests that hyperbaric oxygen treatment has been successfully used to treat deteriorating, severely hypoxemic patients with severe COVID-19.[670] [671] Clinical trials are currently recruiting.[672] [673]

## Nitric oxide

Studies indicate that nitric oxide may help to reduce respiratory tract infection by inactivating viruses and inhibiting their replication in epithelial cells.[674] The FDA has approved an investigational drug application for inhaled nitric oxide to be studied in a phase 3 study of up to 500 patients with COVID-19. Other studies are currently recruiting.

## Aviptadil

A synthetic form of vasoactive intestinal peptide (also known as RLF-100) has been granted an expanded access protocol (which makes the treatment available to patients who have exhausted approved therapies and who are not eligible for the current clinical trial of aviptadil) and fast-track designation by the FDA for the treatment of respiratory failure in patients with COVID-19. Intravenous and inhaled formulations are currently in phase 2 and 3 clinical trials in the US.[675] [676] The manufacturer has requested emergency-use authorization from the FDA for the treatment of patients with critical disease and respiratory failure who have exhausted approved therapies, based on the results of a small case-control study.[677]

## Icatibant

A selective bradykinin B2 receptor antagonist. A small exploratory case-control study of 9 people found an association between the administration of icatibant and improved oxygenation, suggesting that administration in the early stages of disease when patients are hypoxic may be beneficial. Treatment strategies that target the kallikrein-kinin system require further investigation in randomized trials for patients with COVID-19.[678]

## Tradipitant

A neurokinin 1 antagonist that is being trialed for the treatment of neurogenic inflammation of the lung secondary to SARS-CoV-2 infection. Interim analysis of the ODYSSEY study found that hospitalized patients improved sooner when treated with tradipitant compared with placebo. The trial is ongoing.<sup>[679]</sup> <sup>[680]</sup>

# Recommendations

## Monitoring

Regularly monitor the following in hospitalized patients to facilitate early recognition of deterioration and monitor for complications:[2] [692]

- Vital signs (temperature, respiratory rate, heart rate, blood pressure, oxygen saturation)
- Hematologic and biochemistry parameters
- Coagulation parameters (D-dimer, fibrinogen, platelet count, prothrombin time)
- ECG
- Chest imaging
- Signs and symptoms of venous or arterial thromboembolism.

Medical early warning scores

- Utilize medical early warning scores that facilitate early recognition and escalation of treatment of deteriorating patients (e.g., National Early Warning Score 2 [NEWS2], Pediatric Early Warning Signs [PEWS]) where possible.[2]
- There are no data on the value of using these scores in patients with COVID-19 in the primary care setting.[874]

Pregnant women

- Monitor vital signs three to four times daily and fetal heart rate in pregnant women with confirmed infection who are symptomatic and admitted to hospital. Perform fetal growth ultrasounds and Doppler assessments to monitor for potential intrauterine growth restriction in pregnant women with confirmed infection who are asymptomatic.[579] Perform fetal growth ultrasound 14 days after resolution of symptoms.[581]

Post-discharge follow-up

- Patients who are discharged from hospital may have immediate and longer-term health needs including physical (e.g., pulmonary and cardiac rehabilitation, tracheostomy wounds, pressure ulcers, dysphagia, chronic cough, fatigue, neuropathy, muscular weakness, long-term risk of chronic respiratory disorders), psychological and neuropsychological (e.g., delirium, cognitive impairment, post-traumatic stress disorder, anxiety, depression), and social (e.g., impaired activities of daily living).[699]
- Guidelines for the respiratory follow-up of patients with COVID-19 pneumonia have been published. Follow-up algorithms depend on the severity of pneumonia, and may include clinical consultation and review (face-to-face or telephone) by a doctor or nurse, chest imaging, pulmonary function tests, echocardiogram, sputum sampling, walk test, and assessment of oxygen saturation.[875]

## Patient instructions

General prevention measures

- Wash hands often with soap and water for at least 20 seconds or an alcohol-based hand sanitizer (that contains at least 60% alcohol), especially after being in a public place, blowing your nose, or coughing/sneezing. Avoid touching the eyes, nose, and mouth with unwashed hands.
- Avoid close contact with people (i.e., maintain a distance of at least 3 feet [1 meter]) including shaking hands, particularly those who are sick, have a fever, or are coughing or sneezing. It is important to note that recommended distances differ between countries (for example, 6 feet [2 meters] is recommended in the US and UK) and you should consult local guidance.

- Practice respiratory hygiene (i.e., cover mouth and nose when coughing or sneezing, discard tissue immediately in a closed bin, and wash hands).
- Stay at home if you are sick, even with mild symptoms, until you recover (except to get medical care)
- Clean and disinfect frequently touched surfaces daily (e.g., light switches, door knobs, countertops, handles, phones).[299] [300]
- [BMJ Learning: Covid-19 – handwashing technique and PPE videos]
- [WHO: coronavirus disease (COVID-19) advice for the public]

#### Face masks

- The World Health Organization (WHO) recommends that people with symptoms of COVID-19 should wear a medical mask, self-isolate, and seek medical advice as soon as possible. The WHO also now encourages the general public to wear medical or cloth masks in specific situations and settings (e.g., areas with known or suspected widespread transmission and limited or no capacity to implement other containment measures such as social distancing, contact tracing, and testing; settings where social distancing cannot be achieved, particularly in vulnerable populations).[77]
- The Centers for Disease Control and Prevention recommends that homemade cloth face coverings can be worn in public settings where social distancing measures are difficult to maintain (e.g., pharmacies, grocery stores), especially in areas where there is significant community transmission.[306]
- [WHO: coronavirus disease (COVID-19) advice for the public – when and how to use masks]
- [CDC: use of masks to help slow the spread of COVID-19 (includes instructions on how to make masks)]
- [Public Health England: how to make a cloth face covering]

#### Travel advice

- Many countries have implemented international travel bans/closed their borders, have issued advice for domestic travel, and are requesting that citizens traveling abroad should come home immediately if they are able to. Some countries are restricting entry to foreign nationals who have been to affected areas in the preceding 14 days, or are enforcing 14-day quarantine periods where the person's health should be closely monitored (e.g., twice-daily temperature readings).
- Consult local guidance for specific travel restriction recommendations in your country:
  - [WHO: coronavirus disease (COVID-19) travel advice]
  - [CDC: coronavirus disease 2019 (COVID-19) – travel]
  - [NaTHNaC: travel health pro]
  - [Public Health England: travel advice – coronavirus (COVID-19)]
  - [Smartraveller Australia: COVID-19]
  - [Government of Canada: coronavirus disease (COVID-19) – travel restrictions, exemptions, and advice]
  - [Ministry of Manpower Singapore: advisories on COVID-19]

#### Pets

- At this time, there is no evidence that companion animals (including pets and other animals) play a significant role in the spread of COVID-19, and the risk of animals spreading COVID-19 to people is considered to be very low. There is no evidence that the virus can spread to people from the skin or fur of companion animals.[876]
- A very small number of pets have been reported to be infected with the virus after close contact with people with confirmed COVID-19; however, thousands of pets have been tested in the US with none testing positive. There is emerging evidence that cats and ferrets are highly susceptible to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, while dogs and other livestock have no or low susceptibility. A tiger tested positive in a zoo and two domestic pet

cats tested positive in New York (both cats were owned by people with suspected or confirmed infection and both fully recovered).[877] [878] [879] [880] Transmission between cats has also been reported.[881]

- Advise patients to limit their contact with their pets and other animals, especially while they are symptomatic. Advise people to not let pets interact with people or animals outside the household, and if a member of the household becomes unwell to isolate them from everyone else, including pets.[882]
- [\[CDC: coronavirus disease 2019 \(COVID-19\) – pets and other animals\]](#)

#### Athletes and highly active people

- Advise asymptomatic patients who test positive not to exercise for 2 weeks after their test result, with slow resumption of activity under the guidance of a healthcare team. Advise mildly symptomatic patients who test positive not to exercise until 2 weeks after symptom resolution and only after a thorough cardiac evaluation. If the assessment is normal, slow resumption of activity under the guidance of a healthcare team can be considered with close monitoring for clinical deterioration.[883]
- Young athletes with moderate symptoms must be asymptomatic for at least 14 days and obtain clearance from their primary care physician before returning to exercise and competition. Any individual with a history of moderate symptoms (e.g., prolonged fever), cardiac symptoms, or other concerning findings on exam should have an electrocardiography performed and potentially be referred to a pediatric cardiologist for further assessment and clearance prior to returning to play sports.[884]

#### Resources

- [\[WHO: coronavirus disease \(COVID-19\) pandemic\]](#)
- [\[CDC: coronavirus \(COVID-19\)\]](#)
- [\[NHS UK: coronavirus \(COVID-19\)\]](#)
- [\[NHS UK: COVID-19 patient rehabilitation booklet\]](#)
- [\[NHS UK: your COVID recovery\]](#)

## Complications

Complications	Timeframe	Likelihood
<b>venous thromboembolism</b>	<b>variable</b>	<b>high</b>
<p>Several studies have found a high incidence of thrombotic complications in patients with COVID-19, even when thromboprophylaxis had been given.[765] The pooled prevalence of venous thromboembolism, pulmonary embolism (with or without deep vein thrombosis), and deep vein thrombosis alone among all hospitalized patients was 26%, 12%, and 14%, respectively. These rates were higher in patients admitted to the intensive care unit compared with general wards.[766]</p> <p>Coagulopathy in COVID-19 has a prothrombotic character, which may explain reports of thromboembolic complications.[767] Patients may be predisposed to venous thromboembolism due to the direct effects of COVID-19, or the indirect effects of infection (e.g., severe inflammatory response, critical illness, traditional risk factors).[533] Thrombotic events may be due to cytokine storm, hypoxic injury, endothelial dysfunction, hypercoagulability, and/or increased platelet activity.[768]</p> <p>The risk factors with the most evidence for being predictive of venous thromboembolism are older age and elevated D-dimer levels.[765] Patients with very high D-dimer levels have the greatest risk of thrombosis and may benefit from active monitoring.[455] [456]</p> <p>If venous thromboembolism is suspected, perform a computed tomographic angiography or ultrasound of the venous system of the lower extremities.[769]</p> <p>Treat patients with a thromboembolic event (or who are highly suspected to have thromboembolic disease if imaging is not possible) with therapeutic doses of anticoagulant therapy as per the standard of care for patients without COVID-19. There are currently insufficient data to recommend either for or against using therapeutic doses of antithrombotic or thrombolytic agents for COVID-19. Patients who require extracorporeal membrane oxygenation or continuous renal replacement therapy, or who have thrombosis of catheters or extracorporeal filters, should be treated with antithrombotic therapy as per the standard institutional protocols for those without COVID-19.[3]</p> <p>Initial parenteral anticoagulation with a low molecular weight heparin or unfractionated heparin is preferred in acutely ill hospitalized patients; however, direct oral anticoagulants may be used provided there is no potential for drug-drug interactions (lead-in therapy with a parenteral anticoagulant is required for dabigatran and edoxaban). Warfarin can be used after overlap with initial parenteral anticoagulation. Parenteral anticoagulation with a low molecular weight heparin or fondaparinux is preferred over unfractionated heparin in critically ill patients. Direct oral anticoagulants are the preferred option in outpatients provided there is no potential for drug-drug interactions, with warfarin considered a suitable alternative. Anticoagulation therapy is recommended for a minimum of 3 months. Thrombolytic therapy is recommended in select patients with pulmonary embolism.[531]</p> <p>A high incidence (14.7%) of asymptomatic deep vein thrombosis was reported in a cohort of patients with COVID-19 pneumonia.[770] An autopsy study of 12 patients revealed deep vein thrombosis in 58% of patients in whom venous thromboembolism was not suspected before death.[771] These studies highlight the importance of having a high suspicion for venous thromboembolism in patients who have signs of coagulopathy, including elevated D-dimer level.</p> <p>While these patients are at higher risk of thrombotic events, they may also be at an elevated risk for bleeding. In a small retrospective study, 11% of patients at high risk of venous thromboembolism also had a high risk of bleeding.[772]</p> <p>Antiphospholipid antibodies and lupus anticoagulant have been detected in a small number of critically ill patients. The presence of these antibodies can rarely lead to thrombotic events in some patients (especially those who are genetically predisposed) that are difficult to differentiate from other causes of multifocal thrombosis. In other patients, antiphospholipid antibodies may be transient and disappear within a few weeks. The significance of this finding is unknown, although it is thought that these antibodies</p>		

Complications	Timeframe	Likelihood
<p>may not be involved in the pathogenesis of venous thromboembolism in patients with severe COVID-19. Anticoagulation should be considered in these patients.[773] [774] [775] [776] [777]</p> <p>It has been suggested that a new term (e.g., COVID-19-associated pulmonary thrombosis, diffuse pulmonary intravascular coagulopathy, or microvascular COVID-19 lung vessels obstructive thrombo-inflammatory syndrome [MicroCLOTS]) be used rather than the term pulmonary embolism as it has been hypothesized that the pathophysiology is different; local thrombi are formed in the lung vessels due to a local inflammatory process rather than the classical emboli coming from elsewhere in the body.[778] [779] [780] However, this has not become accepted practice.</p> <p>Cases of arterial thrombosis, cerebral venous thrombosis, and acute limb ischemia secondary to thrombosis have been reported.[781] [782] [783] [784] [785]</p>		
<p><b>cardiovascular complications</b></p>	<p><b>variable</b></p>	<p><b>high</b></p>
<p>COVID-19 is associated with a high inflammatory burden that can result in cardiovascular complications with a variety of clinical presentations. Inflammation in the myocardium can result in myocarditis, heart failure, arrhythmias, acute coronary syndrome, rapid deterioration, and sudden death.[786] [787] [788] These complications can occur on presentation or develop as the severity of illness worsens.[789] It is uncertain to what extent acute systolic heart failure is mediated by myocarditis, cytokine storm, small vessel thrombotic complications, microvascular dysfunction, or a variant of stress-induced cardiomyopathy.[790]</p> <p>Cardiac injury has been reported in 24.4% of hospitalized patients, and the all-cause mortality in these patients was 72.6% compared with those without cardiac injury. Factors associated with the development of cardiac injury include older age, chronic obstructive pulmonary disease, and hypertension.[791]</p> <p>Cardiovascular complications have been reported in 14.1% of patients during hospitalization, with an overall case fatality rate of 9.6%. Patients with preexisting cardiovascular comorbidities or risk factors are at higher risk for cardiovascular complications and mortality. Complications include arrhythmias or palpitations (18.4%), myocardial injury (10.3%), angina (10.2%), acute myocardial infarction (3.5%), and acute heart failure (2%).[792] Cases of fulminant myocarditis, cardiac tamponade, cor pulmonale, takotsubo syndrome, and pericarditis have also been reported.[793] [794] [795] [796] [797]</p> <p>Elevated cardiac biomarkers and emerging arrhythmia are associated with the development of severe COVID-19 and the need for intensive care admission.[798]</p> <p>Prevalence of cardiac disease is high among patients who are severely or critically ill, and these patients usually require intensive care and have a poor prognosis and higher rate of in-hospital mortality. These patients are more likely to require noninvasive or invasive ventilation, and have a higher risk of thromboembolic events and septic shock compared with patients without a history of cardiac disease.[789] [799] [800] [801] [802]</p> <p>Perform an ECG and order high-sensitivity troponin I (hs-cTnI) or T (hs-cTnT) and N-terminal pro-brain natriuretic peptide (NT-proBNP) levels in patients with symptoms or signs that suggest acute myocardial injury in order to make a diagnosis. Results should be considered in the clinical context.[803]</p> <p>Monitor blood pressure, heart rate, and fluid balance, and perform continuous ECG monitoring in all patients with suspected or confirmed acute myocardial injury.[803]</p> <p>There are limited data to recommend any specific drug treatments for these patients. Management should involve a multidisciplinary team including intensive care specialists, cardiologists, and infectious disease specialists.[790] It is important to consider that drugs such as hydroxychloroquine and azithromycin may prolong the QT interval and lead to arrhythmias.[803] Guidelines for the management of COVID-19-related myocarditis are available.[804]</p> <p>Infection may have longer-term implications for overall cardiovascular health; however, further research is required.[805] A study of 100 patients who had recently recovered from COVID-19 found that</p>		

Complications	Timeframe	Likelihood
cardiovascular magnetic resonance imaging revealed ongoing myocardial inflammation in 60% of patients, independent of preexisting conditions, severity and overall course of the acute illness, and time from the original diagnosis.[806]		
<b>acute kidney injury</b>	<b>variable</b>	<b>high</b>
<p>The pooled incidence of acute kidney injury is 28.6% among hospitalized patients from the US and Europe, and 5.5% among patients from China. The pooled incidence of renal replacement therapy is 7.7% in the US and Europe, and 2.2% in China. Among patients admitted to the intensive care unit, the incidence of renal replacement therapy is 20.6%. Risk factors associated with acute kidney injury include older age, male sex, cardiovascular disease, diabetes, hypertension, and chronic kidney disease. Acute kidney injury is associated with an increased risk of mortality with a pooled risk ratio of 4.6.[807] Can develop at any time before or during hospital admission.</p> <p>In a small UK cohort, 29% of hospitalized children met the diagnostic criteria for acute kidney injury, with most cases occurring in children admitted to the intensive care unit and in those with pediatric inflammatory multisystem syndrome.[808]</p> <p>Causes include hemodynamic changes, hypovolemia, viral infection leading directly to kidney tubular injury, thrombotic vascular processes, glomerular pathology, or rhabdomyolysis.[809] Direct kidney infection has been confirmed in an autopsy study of a single patient.[810]</p> <p>Patients should meet criteria for acute kidney injury for diagnosis. [NHS England: acute kidney injury (AKI) algorithm] Perform a urinalysis for blood, protein, and glucose to help identify the underlying cause. Imaging is recommended if urinary tract obstruction is suspected.[809]</p> <p>Stop any drugs that can cause or worsen acute kidney injury, if possible. Aim to achieve optimal fluid status (euvoolemia) in all patients. Consider a loop diuretic for treating fluid overload only. Manage hyperkalemia according to local protocols. See local protocols for guidance on renal replacement therapy.[809]</p> <p>Specialist input may be required in some cases (e.g., uncertainty about cause, abnormal urinalysis results, complex fluid management needs, indications for renal replacement therapy), and some patients may require critical care admission.[809] Continuous renal replacement therapy (CRRT) is recommended in critically ill patients with acute kidney injury who develop indications for renal replacement therapy; prolonged intermittent renal replacement therapy is recommended over hemodialysis if CRRT is not available or possible.[3]</p> <p>Monitor fluid status daily, as well as serum blood urea nitrogen, creatinine, and electrolytes at least every 48 hours (or more often if clinically indicated). Monitor patients for the development of, or progression to, chronic kidney disease for at least 2 to 3 years after acute kidney injury.[809]</p> <p>Cases of nephritis and collapsing glomerulopathy have been reported.[811] [812]</p>		
<b>acute liver injury</b>	<b>variable</b>	<b>medium</b>
<p>The pooled prevalence of hepatic manifestations on admission is: elevated alanine aminotransferase (26.6%); elevated aspartate aminotransferase (37.2%); decreased albumin (45.6%); and elevated total bilirubin (18.2%). The incidence of acute hepatic injury was higher in Chinese populations and groups with a higher prevalence of preexisting chronic liver disease; the incidence was similar in younger and older patients. Hepatic complications such as acute hepatic injury have been associated with an increased risk of severe disease and mortality.[813] The prevalence of elevated aspartate aminotransferase was significantly higher in patients with severe disease (45.5%) compared with nonsevere cases (15%).[814]</p> <p>Risk factors associated with severe liver injury include older age, preexisting liver disease, and severe COVID-19.[815]</p>		

Complications	Timeframe	Likelihood
<p>Medications used in the treatment of COVID-19 (e.g., lopinavir/ritonavir) may have a detrimental effect on liver injury.[815]</p> <p>Guidelines on the management of liver derangement in patients with COVID-19 have been published.[816]</p>		
<b>neurologic complications</b>	<b>variable</b>	<b>medium</b>
<p>Patients with severe illness commonly have central or peripheral neurologic complications, possibly due to viral invasion of the central nervous system (severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2] has been detected in the brain and cerebrospinal fluid) or systemic illness.</p> <p>Neurologic symptoms have been reported in 36% to 57% of patients in case series, and were more common in patients with severe illness.[817] [818] However, most studies included minor symptoms such as headache and dizziness, which are classified as symptoms of COVID-19 in this topic rather than complications. In a small retrospective study of patients in an intensive care unit, 44% of patients with neurologic symptoms had abnormal findings on brain magnetic resonance imaging.[819] Neurologic complications are rare in children.[820]</p> <p>Complications include acute cerebrovascular disease, impairment of consciousness, ataxia, neuralgia, seizures, corticospinal tract signs, meningitis, encephalitis, encephalopathy, encephalomyelitis, peripheral demyelinating lesions, peripheral neuropathy, intracerebral hemorrhage, cerebral venous sinus thrombosis, myopathy, myasthenia gravis, and Guillain-Barre syndrome (GBS) and other neuropathies. Patients may present with these signs/symptoms, or they may develop them during the course of the disease.[821] [822]</p> <p>The mean age of patients with GBS was 55 years with a male predominance. Most patients had respiratory and/or severe symptoms of COVID-19, although it has also been reported in asymptomatic patients. A higher prevalence of the classic sensorimotor form and acute inflammatory demyelinating polyneuropathy have been reported, although rare variants have also been noted.[823]</p> <p>Stroke is relatively frequent among hospitalized patients (1.8% for any type of stroke, 1.6% for ischemic stroke) relative to other viral respiratory infections, and has a high risk of in-hospital mortality (34%).[824] Ischemic stroke appears to be more severe and result in worse outcomes (severe disability) in patients with COVID-19, with the median NIH Stroke Scale score being higher among those with COVID-19 compared with those without.[825] Guidelines for the management of acute ischemic stroke in patients with COVID-19 infection have been published.[826]</p> <p>Patients may show cerebral changes on magnetic resonance imaging months after recovery, suggesting that long-term consequences may be possible.[827]</p>		
<b>post-acute COVID-19 (long COVID)</b>	<b>variable</b>	<b>medium</b>
<p>While most patients recover within 2 weeks, approximately 10% of patients still have symptoms after 3 weeks, and some may have symptoms for months, according to data from the UK COVID Symptom Study in which people enter their ongoing symptoms on a smartphone app.[828] The term "long COVID" has been used to describe post-acute COVID-19 symptoms.[829]</p> <p>Nearly 90% of hospitalized patients who recovered from COVID-19 reported persistence of at least one symptom 2 months after discharge. Only 12.6% of patients had no related symptoms, 32% had one or two symptoms, and 55% had three or more symptoms.[830] Prolonged illness can occur among young adults with no underlying comorbidities. In a survey study of symptomatic adults, 35% had not returned to their usual state of health 2 to 3 weeks after testing. Among those ages 18 to 34 years with no underlying chronic medical conditions, 20% had not returned to their usual state of health.[831]</p> <p>Symptoms vary widely, may relapse and remit, and can occur in those with mild disease only. Common long-term symptoms include cough, low-grade fever, and fatigue. Dyspnea, chest pain, myalgia, headaches, rashes, gastrointestinal symptoms, neurocognitive difficulties, and mental health conditions</p>		

Complications	Timeframe	Likelihood
<p>have also been reported. Blood tests should be ordered selectively and for specific clinical indications after a careful history and examination. Other investigations may include chest x-ray, urine tests, and an electrocardiogram.[832]</p> <p>There are no definitive, evidence-based recommendations for the management of post-acute COVID-19 as yet; therefore, patients should be managed pragmatically and symptomatically (e.g., antipyretic for fever, breathing techniques for chronic cough, home pulse oximetry for monitoring breathlessness, pulmonary rehabilitation, staged return to exercise). Many patients recover spontaneously with holistic support, rest, symptomatic treatment, and a gradual increase in activity. Referral to a specialist may be required in patients where there is clinical concern along with respiratory, cardiac, or neurologic symptoms that are new, persistent, or progressive.[832]</p> <p><a href="#">[BMJ webinar: long COVID – how to define it and how to manage it]</a></p> <p><a href="#">[BMJ: management of post-acute covid-19 in primary care]</a></p>		
<b>septic shock</b>	<b>variable</b>	<b>low</b>
<p>Reported in 4% to 8% of patients in case series.[31] [32] [429] [833]</p> <p>Guidelines for the management of shock in critically ill patients with COVID-19 recommend a conservative fluid strategy (crystalloids preferred over colloids) and a vasoactive agent. Norepinephrine (noradrenaline) is the preferred first-line agent, with vasopressin or epinephrine (adrenaline) considered suitable alternatives. Vasopressin can be added to norepinephrine if target mean arterial pressure cannot be achieved with norepinephrine alone.[3] [519] Dopamine is only recommended as an alternative vasopressor in certain patients (e.g., those with a low risk of bradycardia or tachyarrhythmias). Dobutamine is recommended in patients who show evidence of persistent hypoperfusion despite adequate fluid loading and the use of vasopressors. Low-dose corticosteroid therapy is recommended for refractory shock.[3]</p>		
<b>disseminated intravascular coagulation</b>	<b>variable</b>	<b>low</b>
<p>Disseminated intravascular coagulation (DIC) is a manifestation of coagulation failure, and an intermediate link in the development of multi-organ failure. Patients may be at high risk of bleeding/hemorrhage or venous thromboembolism.[834] Reported in 71% of nonsurvivors.[835]</p> <p>Coagulopathy manifests as elevated fibrinogen, elevated D-dimer, and minimal change in prothrombin time, partial thromboplastin time, and platelet count in the early stages of infection. Increasing interleukin-6 levels correlate with increasing fibrinogen levels. Coagulopathy appears to be related to severity of illness and the resultant thromboinflammation. Monitor D-dimer level closely.[836]</p> <p>Prophylactic-dose low molecular weight heparin should be considered in all hospitalized patients with COVID-19 (including those who are not critically ill), unless there are contraindications. This will also protect against venous thromboembolism.[692] Anticoagulant therapy with a low molecular weight heparin or unfractionated heparin has been associated with a better prognosis in patients with severe COVID-19 who have a sepsis-induced coagulopathy (SIC) score of <math>\geq 4</math> or a markedly elevated D-dimer level.[837] In patients with heparin-induced thrombocytopenia (or a history of it), argatroban or bivalirudin are recommended.[834]</p> <p>Standard guidance for the management of bleeding manifestations associated with DIC or septic coagulopathy should be followed if bleeding occurs; however, bleeding manifestations without other associated factors is rare.[692] [836]</p>		
<b>acute respiratory failure</b>	<b>variable</b>	<b>low</b>
<p>Reported in 8% of patients in case series.[32]</p>		

Complications	Timeframe	Likelihood
<p>Leading cause of mortality in patients with COVID-19.[740]</p> <p>Children can quickly progress to respiratory failure.[8]</p>		
<b>cytokine release syndrome</b>	<b>variable</b>	<b>low</b>
<p>Cytokine release syndrome may cause ARDS or multiple-organ dysfunction, which may lead to death.[838] Elevated serum proinflammatory cytokines (e.g., tumor necrosis factor alpha, interleukin-2, interleukin-6, interleukin-8, interleukin-10, granulocyte-colony stimulating factor, monocyte chemoattractant protein 1) and inflammatory markers (e.g., C-reactive protein, serum ferritin) have been commonly reported in patients with severe COVID-19. This likely represents a type of virus-induced secondary hemophagocytic lymphohistiocytosis, which may be fatal.[31] [438] [462] [839] Interleukin-6, in particular, has been associated with severe COVID-19 and increased mortality.[840]</p> <p>One study found that patients who require admission to the intensive care unit have significantly higher levels of interleukin-6, interleukin-10, and tumor necrosis factor alpha, and fewer CD4+ and CD8+ T cells.[841]</p> <p>Anti-inflammatory/immunosuppressive treatments (e.g., tocilizumab, Janus kinase inhibitors) are being trialed in COVID-19 patients.[842] See the Emerging section for more information.</p> <p>Cytokine release syndrome has been reported in children, although cases appear to be rare.[843] See the section below on pediatric inflammatory multisystem syndrome.</p>		
<b>pediatric inflammatory multisystem syndrome</b>	<b>variable</b>	<b>low</b>
<p>A rare, but severe condition, reported in children and adolescents approximately 2 to 4 weeks after the onset of COVID-19, likely due to a postinfectious inflammatory process. The syndrome has a strong temporal association with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.[844] [845] [846] Also known as PIMS, multisystem inflammatory syndrome in children (MIS-C), pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS), as well as other variations.</p> <p>The syndrome shares common features with Kawasaki disease and toxic shock syndrome, but case definitions vary.[347] [846] [847] [848] Most patients have fever, as well as features of shock, cardiac involvement (e.g., elevated cardiac markers, congestive heart failure, cardiac dysfunction, myocarditis, coronary artery dilatation or aneurysm, hypotension, pericardial effusion, mitral regurgitation), gastrointestinal symptoms (e.g., abdominal pain, vomiting, diarrhea), and significantly elevated inflammatory markers.[844] [845] Additional clinical and laboratory characteristics including thrombocytopenia, fatigue, headache, myalgia, sore throat, and lymphadenopathy have been suggested to refine the case definition.[14]</p> <p>A systematic review of 35 studies (783 cases) found that the median age of patients was 8.6 years of age, and 55% of patients were male. Comorbidities were reported in 20% of cases, with obesity being the most common. Cardiovascular symptoms (82% of patients were tachycardic and 61% were hypotensive) and gastrointestinal symptoms (71%) were prominent. Rashes were reported in 42% of patients. Respiratory symptoms were infrequent. The proportion of patients with a positive SARS-CoV-2 reverse-transcription polymerase chain reaction (RT-PCR) or serology test result was 59%, and 41% had chest imaging abnormalities. Inflammatory markers were elevated in 83% of patients. Cardiac markers were also elevated in the majority of patients. Approximately 68% of patients required intensive care admission, 63% required inotropic support, and 28% of patients required respiratory support. The mortality rate was 1.5%.[849]</p> <p>In a multicenter observational study in the UK, 78 cases were reported across 21 pediatric intensive care units. The median age was 11 years and 67% were male. Children from minority ethnic backgrounds accounted for 78% of cases. Fever, shock, abdominal pain, vomiting, and diarrhea were the common presenting features. Around 36% had evidence of coronary artery abnormalities. In terms of treatment, 46% required invasive ventilation and 83% required vasopressor support.[850]</p>		

Complications	Timeframe	Likelihood
<p>Management is mainly supportive and involves a multidisciplinary team (pediatric infectious disease, cardiology, rheumatology, critical care). Patients are commonly managed with intravenous immune globulin, vasopressor support, corticosteroids, immune modulators, anticoagulation, antiplatelet therapy, and respiratory support.[844] [845] A national consensus management pathway from the UK is available.[851]</p> <p>While an association between this syndrome and COVID-19 seems plausible based on current evidence, the association is not definitive and further research is required. It is not clear yet whether this syndrome is Kawasaki disease with SARS-CoV-2 as the triggering agent, or whether this is a different syndrome, although increasing evidence suggests that they are two separate syndromes. The syndrome appears to occur in children who have not manifested the early stages of COVID-19, but appears similar to the later phase of COVID-19 in adults.[852] Immunologically, PIMS appears to be a distinct clinical entity from Kawasaki disease as neutrophilia and raised monocyte counts, features of Kawasaki disease, were not observed in one cohort.[853]</p> <p>Cases of COVID-19-associated Kawasaki-like multisystem inflammatory disease have been reported in adults.[854] [855] [856]</p>		
<b>pregnancy-related complications</b>	<b>variable</b>	<b>low</b>
<p>Pregnancy outcome is usually good, although there are little data on exposure during early pregnancy. Risk factors for severe disease in pregnant women include preexisting comorbidities (e.g., chronic hypertension, diabetes), high maternal age, and high body mass index. Pregnant women are more likely to need intensive care unit admission and invasive ventilation, especially those with a preexisting comorbidity. Preterm birth is more common in pregnant women with COVID-19 compared with pregnant women without the disease. Cesarean delivery occurs in approximately 50% of cases, with the most common indication being severe maternal pneumonia or concern about sudden maternal decompensation. Perinatal deaths are rare, and occur in less than 1% of cases. Stillbirths have been reported. Maternal morbidity is similar to that of women of reproductive age.[18] [354]</p> <p>Limited low-quality evidence suggests that the risk of infection in neonates is extremely low. Most infections are acquired in the postpartum period, although congenitally acquired infection has been reported. Unlike children who generally have asymptomatic infection, two-thirds of neonatal cases are symptomatic and a significant proportion require intensive care, although the overall prognosis appears to be excellent.[354] [857]</p>		
<b>aspergillosis</b>	<b>variable</b>	<b>low</b>
<p>Invasive pulmonary aspergillosis has been reported in critically ill patients with moderate to severe ARDS.[858] [859] [860] A prospective observational study found that one third of mechanically ventilated patients with COVID-19 had putative invasive pulmonary aspergillosis.[861]</p> <p>Intubation for more than 7 days may be a risk factor. Other potential risk factors include older age, chronic obstructive pulmonary disease, immunosuppression, critical illness, or use of high-dose corticosteroids. Consider aspergillosis in patients who deteriorate despite optimal supportive care or have other suspicious radiologic or clinical features.[552] [862]</p> <p>Prescribe appropriate antifungal therapy according to local guidelines.[863]</p>		
<b>pancreatic injury</b>	<b>variable</b>	<b>low</b>
<p>Mild pancreatic injury (defined as elevated serum amylase or lipase levels) has been reported in 17% of patients in one case series.[864] It is unknown whether this is a direct viral effect or due to the harmful immune response that occurs in some patients. Clinical acute pancreatitis has not been reported.[865] [866] Prior history of pancreatitis does not appear to be a risk factor for pancreatic inflammation in patients with COVID-19.[867]</p>		

Complications	Timeframe	Likelihood
<b>autoimmune hemolytic anemia</b>	<b>variable</b>	<b>low</b>
Warm or cold autoimmune hemolytic anemia (first episode) has been reported in 7 patients after the onset of COVID-19 symptoms and within the timeframe compatible with cytokine release syndrome. Four patients had indolent B lymphoid malignancy. It is unknown whether the hemolytic anemia is related to COVID-19 infection.[868]		
<b>immune thrombocytopenia</b>	<b>variable</b>	<b>low</b>
A small number of cases of immune thrombocytopenia have been reported in patients with COVID-19, including one case report in a 10-year-old child and another in a pregnant woman.[869] [870] [871]		
<b>subacute thyroiditis</b>	<b>variable</b>	<b>low</b>
Cases of subacute thyroiditis have been reported in patients with COVID-19 who require intensive care.[872] The first known case of subacute thyroiditis was reported in an 18-year-old woman. Subacute thyroiditis is a thyroid disease of viral or post-viral origin.[873]		

## Prognosis

### Case fatality rate

The overall global case fatality rate (CFR), defined as the total number of deaths reported divided by the total number of detected cases reported, is currently estimated to be 3.1% based on World Health Organization data as of 21 September 2020. The CFR varies considerably between countries.[711]

The overall CFR in China has been estimated to be 2.3% (0.9% in patients without comorbidities) based on a large case series of 72,314 reported cases from 31 December 2019 to 11 February 2020 (mainly among hospitalized patients).[4] However, another study estimates the CFR in China to be lower at 1.38% (after adjusting the crude estimate for censoring, demography, and under-ascertainment).[712]

The overall cumulative incidence of death 90 days after the start of a study in over 10,000 COVID-19 patients in England was <0.01% in those ages 18 to 39 years, and 0.67% and 0.44% in men and women, respectively, in patients ages 80 years and older. Increased risk of death was associated with factors including increasing age, being male, Black and South Asian ethnicity, and comorbidities such as diabetes, severe asthma, and various other medical conditions.[713]

Reported CFRs need to be interpreted with extreme caution. In pandemics, CFRs tend to start high and then trend downwards as more data becomes available. For example, at the start of the 2009 H1N1 influenza pandemic the CFR varied from 0.1% to 5.1% (depending on the country), but the mortality rate ended up being around 0.02%.[714] [Centre for Evidence-Based Medicine: global COVID-19 case fatality rates]

Factors that affect the CFR include:

- Increased case detection of patients with severe disease
- Testing limitations (some countries are only testing patients who have severe symptoms)
- Testing rates in each country
- Delays between symptom onset and death
- Local factors (e.g., patient demographics, availability and quality of health care, other endemic diseases).

Also, the CFR is based on the number of detected cases and there is currently no set definition of a case. A positive polymerase chain reaction (PCR) result is sometimes the only criterion for a case to be recognized; however, a positive PCR test does not equal COVID-19, or mean that a person is necessarily infected or infectious.[715]

It is important to note that daily death counts need to be interpreted with caution. The number of deaths reported on a particular day may not accurately reflect the number of deaths from the previous day due to delays associated with reporting deaths. This makes it difficult to know whether deaths are falling over time in the short term.[716]

In Italy, the CFR may be higher because Italy has the second oldest population in the world, the highest rates of antibiotic resistance deaths in Europe, and a higher incidence of smoking (a known risk factor for more severe disease). The way COVID-19 related deaths are identified and reported in Italy may have also resulted in an overestimation of cases. Patients who die "with" COVID-19 and patients who die "from" COVID-19 are both counted towards the death toll. Only 12% of death certificates have shown direct causality from COVID-19, while 88% of patients who have died had at least one comorbidity.[714] [717]

The overall CFR appears to be less than that reported for severe acute respiratory syndrome coronavirus (SARS) (10%) and Middle East respiratory syndrome (MERS) (37%).[31] Despite the lower CFR, COVID-19 has so far resulted in more deaths than both SARS and MERS combined.[718]

## Infection fatality rate

The infection fatality rate (IFR) is the proportion of deaths among all infected individuals including confirmed cases, undiagnosed cases (e.g., mildly symptomatic or asymptomatic cases), and unreported cases. While the CFR is subject to selection bias as more severe/hospitalized cases are tested, the IFR gives a more accurate picture of the lethality of a disease, especially as testing becomes more rigorous within a population. The Centers for Disease Control and Prevention's current best estimate of the overall IFR is 0.65%.[107]

Among people on board the Diamond Princess cruise ship, a unique situation where an accurate assessment of the IFR in a quarantined population can be made, the IFR was 0.85%. However, all deaths occurred in patients >70 years of age, and the rate in a younger, healthier population could be much lower.[719]

Evidence from seroprevalence studies suggests that the prevalence of infections is much higher than the official figures suggest, and that the virus is much less lethal than the current global case and death counts indicate.

- UK: data from the first round of results of the UK Biobank COVID-19 antibody study indicate that 7.1% of participants had been infected previously overall. Previous infection was most common among people who lived in London (10.4%), and least common among those who lived in the south west of England and Scotland (4.4% in both).[720] Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibodies were measured in the community at an overall adjusted prevalence of 6% in England (20 June to 13 July 2020).[721]
- US: seroprevalence estimates for 10 sites in the US (Connecticut, Louisiana, Minnesota, Missouri, New York City metro area, Philadelphia, San Francisco Bay Area, South Florida, Utah, and Western Washington State) are available from the Centers for Disease Control and Prevention. In the New York City metro area, the number of estimated infections is at least 7 times higher than the number of cases reported according to the latest figures reported for the period 15 to 21 June.[722] [CDC: commercial laboratory seroprevalence survey data]
- Spain: seroprevalence estimates from a nationwide study indicate a seroprevalence of around 5%, with the prevalence in hotspots (e.g., Madrid) being five times higher than that in low-risk regions.[723]
- Switzerland: seroprevalence data from Geneva indicate an IFR of 0.64% for the total population, and an IFR of 0.0092% for people ages 20 to 49 years, 0.14% for people ages 50 to 64 years, and 5.6% for people ages 65 years and older.[724]
- Iran: the seroprevalence estimate after adjusting for population and test performance characteristics in Guilan province was 22% to 33%, resulting in an estimated IFR of 0.08% to 0.12%.[725]

- Denmark: a seroprevalence study in blood donors estimates the IFR to be approximately 0.08% in people aged under 70 years.[726]
- Los Angeles county, California: based on results of the first round of testing, a research team estimates that approximately 2.8% to 5.6% of the county's adult population has antibodies to the virus, an estimated IFR of 0.1% to 0.2% based on current deaths in the county.[727] Published seroprevalence data from adults in Los Angeles county found that the community prevalence of SARS-CoV-2 antibodies was 4.65% in early April. Based on this figure, the authors estimate that approximately 367,000 county residents had SARS-CoV-2 antibodies. This is much higher than the number of confirmed infections at this time, which was 8430. They conclude that fatality rates based on the number of confirmed cases may be much higher than the rates based on the actual number of infections.[728]
- Santa Clara county, California: an analysis of 3300 people in early April found that the seroprevalence of antibodies to SARS-CoV-2 in Santa Clara county was between 2.49% and 4.16%. Based on this, researchers estimate that between 48,000 and 81,000 people were infected with the virus at the time (out of the county's population of approximately 2 million people). Researchers estimate an IFR of 0.1% to 0.2% based on this data.[729]
- Germany: the overall seroprevalence in healthcare workers in a tertiary hospital was low (1.6%).[730]
- Iceland: the country where the most testing per capita has occurred - the IFR lies between 0.01% and 0.19%.[714] A more recent study found that the incidence of infection in Iceland was 0.9%, and the IFR was 0.3%.[731]
- China: seropositivity varied between 3.2% and 3.8% in Wuhan, and decreased in other Chinese cities as the distance to the epicenter increased.[732]

These estimates are likely to change as more data emerge.

## Case fatality rate according to age and presence of comorbidities

The CFR increases with age.[712] The presence of comorbidities is associated with greater disease severity and poor clinical outcomes, and the risk increases with the number of comorbidities a patient has.[733]

The majority of deaths in China have been in patients ages 60 years and older and/or those who have preexisting underlying health conditions (e.g., hypertension, diabetes, cardiovascular disease). The CFR was highest among critical cases (49%). It was also higher in patients ages 80 years and older (15%), males (2.8% versus 1.7% for females), and patients with comorbidities (10.5% for cardiovascular disease, 7.3% for diabetes, 6.3% for chronic respiratory disease, 6% for hypertension, and 5.6% for cancer).[4] Another study found the CFR in China to be 6.4% in patients ages  $\geq 60$  years versus 0.32% in patients ages  $< 60$  years, and 13.4% in patients ages  $\geq 80$  years.[712]

In Italy, the CFR was 8.5% in patients ages 60 to 69 years, 35.5% in patients ages 70 to 79 years, and 52.5% in patients ages  $\geq 80$  years.[734] In a case series of 1591 critically ill patients in Lombardy, the majority of patients were older men, a large proportion required mechanical ventilation and high levels of positive end-expiratory pressure, and the mortality rate in the intensive care unit was 26%.[735]

In the US, the CFR was highest among patients ages  $\geq 85$  years (10% to 27%), followed by those ages 65 to 84 years (3% to 11%), 55 to 64 years (1% to 3%), 20 to 54 years ( $< 1\%$ ), and  $\leq 19$  years (no deaths). Patients ages  $\geq 65$  years accounted for 80% of deaths.[7] The CFR among critically ill patients admitted to the intensive care unit reached 67% in one hospital in Washington state. Most of these patients had underlying health conditions, with congestive heart failure and chronic kidney disease being the most common.[736] The CFR in residents in a long-term care facility in Washington was reported to be 34%.[737]

The case fatality rate in patients with cancer was 37% for patients with hematologic malignancies and 25% for solid malignancies in one study. Some 55% of lung cancer patients died from COVID-19.[738]

Children have a good prognosis and generally recover within 1 to 2 weeks, and deaths are rare.[17] In one study, approximately 75% of COVID-19-related deaths in young people under the age of 21 years in the US occurred in those with underlying health conditions, most commonly asthma, obesity, neurologic/developmental conditions, and cardiovascular conditions. The majority of deaths occurred in those ages 10 to 20 years (70%), with 20% of deaths in those ages 1 to 9 years, and 10% in infants under 1 year of age. Hispanic, non-Hispanic Black, and non-Hispanic American Indian/Alaskan Native people accounted for 78% of deaths.[739]

## Prognostic factors

The leading cause of death in patients with COVID-19 is respiratory failure from acute respiratory distress syndrome.[740] The overall pooled mortality rate from acute respiratory distress syndrome in COVID-19 patients is 39%; however, this varies significantly between countries (e.g., China 69%, Iran 28%, France 19%, Germany 13%).[741] Patients who required invasive mechanical ventilation had an 88% mortality rate in one study in New York, but it has been much lower (36% to 53%) in other studies.[742] [743] [744] The other most common complications in deceased patients are myocardial injury, liver or kidney injury, and multi-organ dysfunction.[745] The strongest predictor of in-hospital mortality was chronic pulmonary disease, followed by chronic cardiovascular disease, older age, and elevated interleukin-6 and D-dimer levels at admission in a New York study.[551] In one retrospective study of 52 critically ill patients in Wuhan City, 61.5% of patients died by 28 days, and the median time from admission to the intensive care unit to death was 7 days for patients who didn't survive.[746]

Prognostic factors that have been associated with increased risk of unfavorable outcomes and mortality include:[747]

- Age  $\geq$ 50 years
- Male sex
- Smoking
- Presence of comorbidities (e.g., hypertension, diabetes, cardiovascular or cerebrovascular disease, COPD, obesity, malignancy)
- Lymphopenia
- Thrombocytopenia
- Liver, kidney impairment, or cardiac injury
- Elevated inflammatory markers (C-reactive protein, procalcitonin, ferritin)
- Elevated D-dimer
- Elevated interleukin-6.

The most common risk factors for death are age  $\geq$ 65 years, male sex, hypertension, cardiovascular disease, diabetes, chronic obstructive pulmonary disease, and cancer.[748]

## Prognostic scores

The APACHE II score was found to be an effective clinical tool to predict hospital mortality in patients with COVID-19, and performed better than SOFA and CURB-65 scores in a small retrospective observational study. An APACHE II score of 17 or more was an early indicator of death and may help provide guidance to make further clinical decisions.[749] In another retrospective study, A-DROP (a modified version of CURB-65) showed better accuracy of in-hospital death prediction on admission compared with other widely used community-acquired pneumonia scores.[750] Further research is required to confirm these findings, and to validate the use of prognostic scores in patients with COVID-19.

New clinical risk scores to predict disease progression and the risk for critical illness in hospitalized patients with COVID-19 have been developed (e.g., COVID-GRAM, CALL score).[751] [752] COVID-GRAM, a web-based calculator to estimate the probability that a patient will develop critical illness (defined as intensive care admission, invasive ventilation, or death) has been validated in a study of nearly 1600 patients in China. It relies on the following 10 variables at admission: chest radiographic abnormality, age, hemoptysis, dyspnea, unconsciousness, number of comorbidities, cancer history, neutrophil-to-lymphocyte ratio, lactate dehydrogenase, and direct bilirubin. Additional validation studies, especially outside of China, are required.[752]

The 4C (Coronavirus Clinical Characterisation Consortium) Mortality Score was developed and validated in a UK prospective cohort study of nearly 60,000 adults admitted to hospital with COVID-19. The score uses patient demographics, clinical observations, and blood parameters commonly available at the time of hospital admission (i.e., age, sex, number of comorbidities, respiratory rate, peripheral oxygen saturation, Glasgow Coma Scale score, urea, C-reactive protein), and can accurately characterize patients as being at low, intermediate, high, or very high risk of death. The score outperformed other risk stratification tools,

showed clinical decision-making utility, and had similar performance to more complex models. The score should be further validated to determine its applicability in other populations.[753]

## Refractory disease

Refractory disease (patients who do not reach obvious clinical and radiologic remission within 10 days after hospitalization) has been reported in nearly 50% of hospitalized patients in one retrospective single-center study of 155 patients in China. Risk factors for refractory disease include older age, male sex, and the presence of comorbidities. These patients generally require longer hospital stays as their recovery is slower.[754]

## Infectivity of recovered cases

Potential infectivity of recovered cases is still unclear. There have been case reports of patients testing positive again after being discharged. This suggests that some patients in convalescence may still be contagious, although this is yet to be confirmed.[755] [756]

## Reinfection

There is limited information about reinfection. Recurrent RT-PCR positivity in patients 1 to 60 days after recovery ranges between 7% to 23% in studies, with an estimated pooled rate of 12%.[757] It is currently unclear whether this is due to reinfection, persistent viral shedding, or whether the test result was a false-negative at the time of discharge.

Studies have repeatedly reported positive RT-PCR tests for up to 90 days after initial infection; therefore, it is most likely that these cases are actually protracted initial infections. It is important to note that although persistent viral shedding has been reported for up to 90 days after the onset of infection, replication-competent virus has not been identified 10 to 20 days after the onset of symptoms (depending on disease severity).[758]

More recently a man from Hong Kong is reported to have the first confirmed case of reinfection; the patient's two symptomatic episodes (4.5 months apart) were caused by virus strains with different genomic sequences.[759]

## Postinfection immunity

Evidence is currently insufficient to know whether individuals with SARS-CoV-2 antibodies have protective immunity.[399] A study in macaques suggests that infection with SARS-CoV-2 offers protection against reinfection.[760] Limited data suggest that recovery from COVID-19 might confer immunity against reinfection in humans, too.[761] Most convalescent patients have detectable neutralizing antibodies and cellular immune responses.[762] In a study of over 1200 patients who recovered from confirmed COVID-19 in Iceland, over 90% of patients tested positive for SARS-CoV-2 antibodies; antibody levels increased during the 2 months after diagnosis and then plateaued, remaining stable over the next 2 months.[731] Among 175 patients who recovered from mild disease in China, neutralizing antibody titers to SARS-CoV-2 varied substantially.[763] There are data to suggest that asymptomatic people may have a weaker immune response to infection; however, this is yet to be confirmed.[764]



# Diagnostic guidelines

## International

### Overview of testing for SARS-CoV-2 (COVID-19) [384]

**Published by:** Centers for Disease Control and Prevention

**Last published:** 2020

### Interim guidelines for collecting, handling, and testing clinical specimens for COVID-19 [389]

**Published by:** Centers for Disease Control and Prevention

**Last published:** 2020

### Interim guidelines for COVID-19 antibody testing [400]

**Published by:** Centers for Disease Control and Prevention

**Last published:** 2020

### Interim infection prevention and control recommendations for healthcare personnel during the coronavirus disease 2019 (COVID-19) pandemic [483]

**Published by:** Centers for Disease Control and Prevention

**Last published:** 2020

### Infectious Diseases Society of America guidelines on the diagnosis of COVID-19 [484]

**Published by:** Infectious Diseases Society of America

**Last published:** 2020

### Infectious Diseases Society of America guidelines on the diagnosis of COVID-19: serologic testing [401]

**Published by:** Infectious Diseases Society of America

**Last published:** 2020

### Infectious Diseases Society of America guidelines on infection prevention in patients with suspected or known COVID-19 [485]

**Published by:** Infectious Diseases Society of America

**Last published:** 2020

### COVID-19 real-time learning network [486]

**Published by:** Infectious Diseases Society of America

**Last published:** 2020

### Clinical guidance [487]

**Published by:** American Academy of Pediatrics

**Last published:** 2020

### Country & technical guidance - coronavirus disease (COVID-19) [488]

**Published by:** World Health Organization

**Last published:** 2020

### Diagnostic testing for SARS-CoV-2: interim guidance [345]

**Published by:** World Health Organization

**Last published:** 2020

### Antigen-detection in the diagnosis of SARS-CoV-2 infection using rapid immunoassays: interim guidance [407]

**Published by:** World Health Organization

**Last published:** 2020

## International

### Public health surveillance for COVID-19: interim guidance [153]

**Published by:** World Health Organization

**Last published:** 2020

### Infection prevention and control during health care when coronavirus disease (COVID-19) is suspected or confirmed: interim guidance [295]

**Published by:** World Health Organization

**Last published:** 2020

### Use of chest imaging in COVID-19: a rapid advice guide [410]

**Published by:** World Health Organization

**Last published:** 2020

### Assessment of COVID-19 in primary care [489]

**Published by:** Scottish Intercollegiate Guidelines Network

**Last published:** 2020

### COVID-19 position statement: presentations and management of COVID-19 in older people in acute care [490]

**Published by:** Scottish Intercollegiate Guidelines Network

**Last published:** 2020

### COVID-19: guidance for health professionals [491]

**Published by:** Public Health England

**Last published:** 2020

### COVID-19 pandemic [492]

**Published by:** European Centre for Disease Prevention and Control

**Last published:** 2020

### A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia [493]

**Published by:** Zhongnan Hospital of Wuhan University Novel Coronavirus Management and Research Team; Evidence-Based Medicine Chapter of China International Exchange and Promotive Association for Medical and Health Care

**Last published:** 2020

### Diagnosis and clinical management of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection [494]

**Published by:** Peking Union Medical College Hospital

**Last published:** 2020

# Treatment guidelines

## International

### Coronavirus disease 2019 (COVID-19) treatment guidelines [3]

**Published by:** National Institutes of Health

**Last published:** 2020

### Information for healthcare professionals about coronavirus (COVID-19) [681]

**Published by:** Centers for Disease Control and Prevention

**Last published:** 2020

### Interim clinical guidance for management of patients with confirmed coronavirus disease (COVID-19) [682]

**Published by:** Centers for Disease Control and Prevention

**Last published:** 2020

### Information for clinicians on investigational therapeutics for patients with COVID-19 [683]

**Published by:** Centers for Disease Control and Prevention

**Last published:** 2020

### Interim guidance for implementing home care of people not requiring hospitalization for coronavirus disease 2019 (COVID-19) [684]

**Published by:** Centers for Disease Control and Prevention

**Last published:** 2020

### Discontinuation of transmission-based precautions and disposition of patients with COVID-19 in healthcare settings (interim guidance) [516]

**Published by:** Centers for Disease Control and Prevention

**Last published:** 2020

### Discontinuation of isolation for persons with COVID-19 not in healthcare settings [506]

**Published by:** Centers for Disease Control and Prevention

**Last published:** 2020

### Interim U.S. guidance for risk assessment and work restrictions for healthcare personnel with potential exposure to COVID-19 [685]

**Published by:** Centers for Disease Control and Prevention

**Last published:** 2020

### Infectious Diseases Society of America guidelines on the treatment and management of patients with COVID-19 [499]

**Published by:** Infectious Diseases Society of America

**Last published:** 2020

### COVID-19: interim guidance on management pending empirical evidence [566]

**Published by:** American Thoracic Society

**Last published:** 2020

### COVID-19 real-time learning network [486]

**Published by:** Infectious Diseases Society of America

**Last published:** 2020

## International

### Prevention, diagnosis, and treatment of VTE in patients with coronavirus disease 2019 [531]

**Published by:** CHEST Guideline and Expert Panel

**Last published:** 2020

### Thromboembolism and anticoagulant therapy during the COVID-19 pandemic: interim clinical guidance from the Anticoagulation Forum [530]

**Published by:** Anticoagulation Forum

**Last published:** 2020

### Evaluation and management considerations for neonates at risk for COVID-19 [584]

**Published by:** Centers for Disease Control and Prevention

**Last published:** 2020

### Clinical guidance [487]

**Published by:** American Academy of Pediatrics

**Last published:** 2020

### Caring for children and youth with special health care needs during the COVID-19 pandemic [686]

**Published by:** American Academy of Pediatrics

**Last published:** 2020

### Management of infants born to mothers with suspected or confirmed COVID-19 [582]

**Published by:** American Academy of Pediatrics

**Last published:** 2020

### Novel coronavirus 2019 (COVID-19) [578]

**Published by:** American College of Obstetricians and Gynecologists

**Last published:** 2020

### Coronavirus disease (COVID-19): outbreak update [687]

**Published by:** Government of Canada

**Last published:** 2020

### Country & technical guidance - coronavirus disease (COVID-19) [488]

**Published by:** World Health Organization

**Last published:** 2020

### Clinical management of COVID-19: interim guidance [2]

**Published by:** World Health Organization

**Last published:** 2020

### Home care for patients with suspected or confirmed COVID-19 and management of their contacts: interim guidance [688]

**Published by:** World Health Organization

**Last published:** 2020

### Criteria for releasing COVID-19 patients from isolation: scientific brief [689]

**Published by:** World Health Organization

**Last published:** 2020

### Advice on the use of masks in the context of COVID-19: interim guidance [77]

**Published by:** World Health Organization

**Last published:** 2020

## International

### Rapid advice guidelines for management of children with COVID-19 [690]

**Published by:** International multidisciplinary working group

**Last published:** 2020

### COVID-19 guidance and the latest research in the Americas [691]

**Published by:** Pan American Health Organization

**Last published:** 2020

### ISTH interim guidance on recognition and management of coagulopathy in COVID-19 [692]

**Published by:** International Society of Thrombosis and Haemostasis

**Last published:** 2020

### Surviving Sepsis Campaign: guidelines on the management of critically ill adults with coronavirus disease 2019 (COVID-19) [519]

**Published by:** Surviving Sepsis Campaign

**Last published:** 2020

### Labor and delivery guidance for COVID-19 [693]

**Published by:** International working group

**Last published:** 2020

### Global interim guidance on coronavirus disease 2019 (COVID-19) during pregnancy and puerperium from FIGO and allied partners: information for healthcare professionals [408]

**Published by:** International Federation of Gynecology and Obstetrics

**Last published:** 2020

### ISUOG interim guidance on coronavirus disease 2019 (COVID-19) during pregnancy and puerperium: information for healthcare professionals – an update [694]

**Published by:** International Society of Ultrasound in Obstetrics and Gynecology

**Last published:** 2020

### Coronavirus specialty guides [695]

**Published by:** NHS England

**Last published:** 2020

### COVID-19 rapid guideline: critical care in adults [495]

**Published by:** National Institute for Health and Care Excellence (UK)

**Last published:** 2020

### Coronavirus (COVID-19): rapid guidelines and evidence reviews [696]

**Published by:** National Institute for Health and Care Excellence (UK)

**Last published:** 2020

### COVID-19: guidance for health professionals [491]

**Published by:** Public Health England

**Last published:** 2020

### BMJ's coronavirus (covid-19) hub [697]

**Published by:** BMJ

**Last published:** 2020

## International

### COVID-19#pandemic [492]

**Published by:** European Centre for Disease Prevention and Control

**Last published:** 2020

### COVID-19: information for the respiratory community [698]

**Published by:** British Thoracic Society

**Last published:** 2020

### COVID-19 position statement: presentations and management of COVID-19 in older people in acute care [490]

**Published by:** Scottish Intercollegiate Guidelines Network

**Last published:** 2020

### After-care needs of inpatients recovering from COVID-19 [699]

**Published by:** NHS England

**Last published:** 2020

### Community palliative, end of life and bereavement care in the COVID-19 pandemic [700]

**Published by:** Royal College of General Practitioners; Association for Palliative Medicine

**Last published:** 2020

### Coronavirus (COVID-19) infection in pregnancy [581]

**Published by:** Royal College of Obstetricians and Gynaecologists (UK)

**Last published:** 2020

### Recommendations on the clinical management of the COVID-19 infection by the new coronavirus SARS-CoV2 [701]

**Published by:** Spanish Paediatric Association

**Last published:** 2020

### Management of critically ill patients with COVID-19 in ICU: statement from front-line intensive care experts in Wuhan, China [702]

**Published by:** Chinese expert working panel

**Last published:** 2020

### Coronavirus disease [703]

**Published by:** Chinese Center for Disease Control and Prevention

**Last published:** 2020

### Handbook of COVID-19 prevention and treatment [704]

**Published by:** First Affiliated Hospital, Zhejiang University School of Medicine

**Last published:** 2020

### A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia [493]

**Published by:** Zhongnan Hospital of Wuhan University Novel Coronavirus Management and Research Team; Evidence-Based Medicine Chapter of China International Exchange and Promotive Association for Medical and Health Care

**Last published:** 2020

## International

### Diagnosis and treatment protocol for novel coronavirus pneumonia (trial version 7) [705]

**Published by:** National Health Commission of the People's Republic of China; National Administration of Traditional Chinese Medicine of the People's Republic of China

**Last published:** 2020

### Diagnosis and clinical management of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection [494]

**Published by:** Peking Union Medical College Hospital

**Last published:** 2020

### Updates on COVID-19 (coronavirus disease 2019) local situation [706]

**Published by:** Ministry of Health Singapore

**Last published:** 2020

### New coronavirus infectious disease (COVID-19) related information page [707]

**Published by:** National Institute of Infectious Diseases Japan

**Last published:** 2020

### COVID-19 infection [708]

**Published by:** Japanese Association for Infectious Diseases

**Last published:** 2020

### Perinatal and neonatal management plan for prevention and control of SARS-CoV-2 infection (2nd edition) [709]

**Published by:** Working Group for the Prevention and Control of Neonatal SARS-CoV-2 Infection in the Perinatal Period of the Editorial Committee of Chinese Journal of Contemporary Pediatrics

**Last published:** 2020

### Coronavirus disease 2019 (COVID-19) [710]

**Published by:** Department of Health Australia

**Last published:** 2020

## Online resources

1. [American Academy of Pediatrics: children and COVID-19 – state-level data report](#) (*external link*)
2. [Johns Hopkins University: coronavirus COVID-19 global cases](#) (*external link*)
3. [BMJ talk medicine podcast: Covid-19 update](#) (*external link*)
4. [BMJ Best Practice: Management of coexisting conditions in the context of COVID-19](#) (*external link*)
5. [WHO: coronavirus disease \(COVID-19\) emergency dashboard](#) (*external link*)
6. [WHO: coronavirus disease \(COVID-2019\) weekly epidemiological updates](#) (*external link*)
7. [CDC: COVIDView](#) (*external link*)
8. [GenBank](#) (*external link*)
9. [WHO: infection prevention and control during health care when coronavirus disease \(COVID-19\) is suspected or confirmed](#) (*external link*)
10. [CDC: interim infection prevention and control recommendations for healthcare personnel during the coronavirus disease 2019 \(COVID-19\) pandemic](#) (*external link*)
11. [BMJ: covid-19 – PPE guidance](#) (*external link*)
12. [BMJ: covid-19 in primary care \(UK\)](#) (*external link*)
13. [BMJ: covid-19 – a remote assessment in primary care](#) (*external link*)
14. [BMJ Learning: Covid-19 – handwashing technique and PPE videos](#) (*external link*)
15. [WHO: coronavirus disease \(COVID-19\) advice for the public](#) (*external link*)
16. [Centre for Evidence-Based Medicine: what is the evidence to support the 2-metre social distancing rule to reduce COVID-19 transmission?](#) (*external link*)
17. [BMJ: facemasks for the prevention of infection in healthcare and community settings](#) (*external link*)
18. [BMJ: analysis – face masks for the public during the covid-19 crisis](#) (*external link*)
19. [Public Health England: coronavirus \(COVID-19\) – how to self-isolate when you travel to the UK](#) (*external link*)
20. [Public Health England: staying alert and safe \(social distancing\)](#) (*external link*)

21. [Public Health England: guidance on shielding and protecting people who are clinically extremely vulnerable from COVID-19 \(external link\)](#)
22. [Public Health England: guidance for young people on shielding and protecting people most likely to become unwell if they catch coronavirus \(external link\)](#)
23. [Royal College of Paediatrics and Child Health: COVID-19 – ‘shielding’ guidance for children and young people \(external link\)](#)
24. [Public Health England: COVID-19 – advice for smokers and vapers \(external link\)](#)
25. [BMJ practice pointer: testing for SARS-CoV-2 antibodies \(external link\)](#)
26. [BSTI: radiology decision tool for suspected COVID-19 \(external link\)](#)
27. [BSTI: lung ultrasound \(LUS\) for COVID-19 patients in critical care areas \(external link\)](#)
28. [WHO: public health surveillance for COVID-19 – interim guidance \(external link\)](#)
29. [CDC: coronavirus disease 2019 \(COVID-19\) 2020 interim case definition \(external link\)](#)
30. [PHE: COVID-19 – investigation and initial clinical management of possible cases \(external link\)](#)
31. [ECDC: case definition for coronavirus disease 2019 \(COVID-19\) \(external link\)](#)
32. [WHO: home care for patients with suspected or confirmed COVID-19 and management of their contacts \(external link\)](#)
33. [CDC: interim guidance for implementing home care of people not requiring hospitalization for coronavirus disease 2019 \(COVID-19\) \(external link\)](#)
34. [Clinical frailty scale \(external link\)](#)
35. [NICE: COVID-19 prescribing brief – corticosteroids \(external link\)](#)
36. [BMJ interactive tool: drug treatments for covid-19 – living systematic review and network meta-analysis \(external link\)](#)
37. [BMJ rapid recommendations: a living WHO guideline on drugs for COVID-19 \(external link\)](#)
38. [BMJ rapid recommendations: remdesivir for severe covid-19 – a clinical practice guideline \(external link\)](#)
39. [ACOG: outpatient assessment and management for pregnant women with suspected or confirmed novel coronavirus \(COVID-19\) \(external link\)](#)
40. [Global coronavirus COVID-19 clinical trial tracker \(external link\)](#)

41. [WHO: off-label use of medicines for COVID-19 \(external link\)](#)
42. [WHO: “Solidarity” clinical trial for COVID-19 treatments \(external link\)](#)
43. [RECOVERY trial \(external link\)](#)
44. [Centre for Evidence-Based Medicine: lopinavir/ritonavir – a rapid review of effectiveness in COVID-19 \(external link\)](#)
45. [Centre for Evidence-Based Medicine: global COVID-19 case fatality rates \(external link\)](#)
46. [CDC: commercial laboratory seroprevalence survey data \(external link\)](#)
47. [NHS England: acute kidney injury \(AKI\) algorithm \(external link\)](#)
48. [BMJ webinar: long COVID – how to define it and how to manage it \(external link\)](#)
49. [BMJ: management of post-acute covid-19 in primary care \(external link\)](#)
50. [WHO: coronavirus disease \(COVID-19\) advice for the public – when and how to use masks \(external link\)](#)
51. [CDC: use of masks to help slow the spread of COVID-19 \(includes instructions on how to make masks\) \(external link\)](#)
52. [Public Health England: how to make a cloth face covering \(external link\)](#)
53. [WHO: coronavirus disease \(COVID-19\) travel advice \(external link\)](#)
54. [CDC: coronavirus disease 2019 \(COVID-19\) – travel \(external link\)](#)
55. [NaTHNaC: travel health pro \(external link\)](#)
56. [Public Health England: travel advice – coronavirus \(COVID-19\) \(external link\)](#)
57. [Smartraveller Australia: COVID-19 \(external link\)](#)
58. [Government of Canada: coronavirus disease \(COVID-19\) – travel restrictions, exemptions, and advice \(external link\)](#)
59. [Ministry of Manpower Singapore: advisories on COVID-19 \(external link\)](#)
60. [CDC: coronavirus disease 2019 \(COVID-19\) – pets and other animals \(external link\)](#)
61. [WHO: coronavirus disease \(COVID-19\) pandemic \(external link\)](#)
62. [CDC: coronavirus \(COVID-19\) \(external link\)](#)

63. [NHS UK: coronavirus \(COVID-19\) \(external link\)](#)
64. [NHS UK: COVID-19 patient rehabilitation booklet \(external link\)](#)
65. [NHS UK: your COVID recovery \(external link\)](#)

## Key articles

## References

1. Coronaviridae Study Group of the International Committee on Taxonomy of Viruses. The species severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. *Nat Microbiol.* 2020 Apr;5(4):536-44. [Full text](#) [Abstract](#)
2. World Health Organization. Clinical management of COVID-19: interim guidance. 2020 [internet publication]. [Full text](#)
3. National Institutes of Health. Coronavirus disease 2019 (COVID-19) treatment guidelines. 2020 [internet publication]. [Full text](#)
4. Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China [in Chinese]. *Zhonghua Liu Xing Bing Xue Za Zhi.* 2020 Feb 17;41(2):145-51. [Full text](#) [Abstract](#)
5. Colaneri M, Sacchi P, Zuccaro V, et al. Clinical characteristics of coronavirus disease (COVID-19) early findings from a teaching hospital in Pavia, North Italy, 21 to 28 February 2020. *Euro Surveill.* 2020 Apr;25(16). [Full text](#) [Abstract](#)
6. Docherty AB, Harrison EM, Green CA, et al. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO clinical characterisation protocol: prospective observational cohort study. *BMJ.* 2020 May 22;369:m1985. [Full text](#) [Abstract](#)
7. CDC COVID-19 Response Team. Severe outcomes among patients with coronavirus disease 2019 (COVID-19): United States, February 12 - March 16, 2020. *MMWR Morb Mortal Wkly Rep.* 2020 Mar 27;69(12):343-6. [Full text](#) [Abstract](#)
8. Dong Y, Mo X, Hu Y, et al. Epidemiology of COVID-19 among children in China. *Pediatrics.* *Pediatrics.* 2020 Jun;145(6):e20200702. [Full text](#) [Abstract](#)
9. Garazzino S, Montagnani C, Donà D, et al. Multicentre Italian study of SARS-CoV-2 infection in children and adolescents, preliminary data as at 10 April 2020. *Euro Surveill.* 2020 May;25(18). [Full text](#) [Abstract](#)
10. Brambilla I, Castagnoli R, Caimmi S, et al. COVID-19 in the pediatric population admitted to a tertiary referral hospital in Northern Italy: preliminary clinical data. *Pediatr Infect Dis J.* 2020 Jul;39(7):e160. [Full text](#) [Abstract](#)
11. Livingston E, Bucher K. Coronavirus disease 2019 (COVID-19) in Italy. *JAMA.* 2020 Apr 14;323(14):1335. [Full text](#) [Abstract](#)
12. Tagarro A, Epalza C, Santos M, et al. Screening and severity of coronavirus disease 2019 (COVID-19) in children in Madrid, Spain. *JAMA Pediatr.* 2020 Apr 8 [Epub ahead of print]. [Full text](#) [Abstract](#)

13. American Academy of Pediatrics. Children and COVID-19: state-level data report. 2020 [internet publication]. [Full text](#)
14. Swann OV, Holden KA, Turtle L, et al. Clinical characteristics of children and young people admitted to hospital with covid-19 in United Kingdom: prospective multicentre observational cohort study. *BMJ*. 2020 Aug 27;370:m3249. [Full text](#)
15. Mehta NS, Mytton OT, Mullins EWS, et al. SARS-CoV-2 (COVID-19): what do we know about children? A systematic review. *Clin Infect Dis*. 2020 May 11 [Epub ahead of print]. [Full text](#) [Abstract](#)
16. Posfay-Barbe KM, Wagner N, Gauthey M, et al. COVID-19 in children and the dynamics of infection in families. *Pediatrics*. 2020 Aug;146(2):e20201576. [Full text](#) [Abstract](#)
17. Castagnoli R, Votto M, Licari A, et al. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children and adolescents: a systematic review. *JAMA Pediatr*. 2020 Apr 22 [Epub ahead of print]. [Full text](#) [Abstract](#)
18. Khalil A, Kalafat E, Benlioglu C, et al. SARS-CoV-2 infection in pregnancy: a systematic review and meta-analysis of clinical features and pregnancy outcomes. *EClinicalMedicine*. 2020 Jul 3:100446. [Full text](#) [Abstract](#)
19. Knight M, Bunch K, Vousden N, et al. Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: national population based cohort study. *BMJ*. 2020 Jun 8;369:m2107. [Full text](#) [Abstract](#)
20. Ellington S, Strid P, Tong VT, et al. Characteristics of women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status: United States, January 22 – June 7, 2020. *MMWR Morb Mortal Wkly Rep*. 2020 Jun 26;69(25):769-75. [Full text](#) [Abstract](#)
21. Gómez-Ochoa SA, Franco OH, Rojas LZ, et al. COVID-19 in healthcare workers: a living systematic review and meta-analysis of prevalence, risk factors, clinical characteristics, and outcomes. *Am J Epidemiol*. 2020 Sep 1 [Epub ahead of print]. [Full text](#) [Abstract](#)
22. Sahu AK, Amrithanand VT, Mathew R, et al. COVID-19 in health care workers: a systematic review and meta-analysis. *Am J Emerg Med*. 2020 Jun 6;38(9):1727-31. [Full text](#) [Abstract](#)
23. Torjesen I. Covid-19: one in 10 cases in England occurred in frontline health and social care staff. *BMJ*. 2020 Jul 7;370:m2717. [Full text](#) [Abstract](#)
24. Kluytmans-van den Bergh MFQ, Buiting AGM, Pas SD, et al. Prevalence and clinical presentation of health care workers with symptoms of coronavirus disease 2019 in 2 Dutch hospitals during an early phase of the pandemic. *JAMA Netw Open*. 2020 May 1;3(5):e209673. [Full text](#) [Abstract](#)
25. CDC COVID-19 Response Team. Characteristics of health care personnel with COVID-19: United States, February 12 –April 9, 2020. *MMWR Morb Mortal Wkly Rep*. 2020 Apr 17;69(15):477-81. [Full text](#) [Abstract](#)
26. Ren LL, Wang YM, Wu ZQ, et al. Identification of a novel coronavirus causing severe pneumonia in human: a descriptive study. *Chin Med J (Engl)*. 2020 May 5;133(9):1015-24. [Full text](#) [Abstract](#)

27. Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med*. 2020 Feb 20;382(8):727-33. [Full text](#) [Abstract](#)
28. Lu R, Zhao X, Li J, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet*. 2020 Feb 22;395(10224):565-74. [Full text](#) [Abstract](#)
29. Tang X, Wu C, Li X, et al. On the origin and continuing evolution of SARS-CoV-2. *Nat Sci Review*. 2020 Mar 3 [Epub ahead of print]. [Full text](#)
30. Young BE, Fong SW, Chan YH, et al. Effects of a major deletion in the SARS-CoV-2 genome on the severity of infection and the inflammatory response: an observational cohort study. *Lancet*. 2020 Aug 18 [Epub ahead of print]. [Full text](#) [Abstract](#)
31. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020 Feb 15;395(10223):497-506. [Full text](#) [Abstract](#)
32. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*. 2020 Feb 15;395(10223):507-13. [Full text](#) [Abstract](#)
33. Li Q, Guan X, Wu P, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med*. 2020 Mar 26;382(13):1199-207. [Full text](#) [Abstract](#)
34. Paraskevis D, Kostaki EG, Magiorkinis G, et al. Full-genome evolutionary analysis of the novel coronavirus (2019-nCoV) rejects the hypothesis of emergence as a result of a recent recombination event. *Infect Genet Evol*. 2020 Jan 29;79:104212. [Abstract](#)
35. Ji W, Wang W, Zhao X, et al. Cross-species transmission of the newly identified coronavirus 2019-nCoV. *J Med Virol*. 2020 Apr;92(4):433-40. [Full text](#) [Abstract](#)
36. Zhang T, Wu Q, Zhang Z. Probable pangolin origin of SARS-CoV-2 associated with the COVID-19 outbreak. *Curr Biol*. 2020 Apr 6;30(7):1346-51. [Full text](#) [Abstract](#)
37. Lam TT, Shum MH, Zhu HC, et al. Identifying SARS-CoV-2 related coronaviruses in Malayan pangolins. *Nature*. 2020 Jul;583(7815):282-5. [Full text](#) [Abstract](#)
38. Mallapaty S. Animal source of the coronavirus continues to elude scientists. *Nature*. 2020 May 18 [Epub ahead of print]. [Full text](#) [Abstract](#)
39. Meyerowitz EA, Richterman A, Gandhi RT, et al. Transmission of SARS-CoV-2: a review of viral, host, and environmental factors. *Ann Intern Med*. 2020 Sep 17 [Epub ahead of print]. [Full text](#) [Abstract](#)
40. World Health Organization. Transmission of SARS-CoV-2: implications for infection prevention precautions – scientific brief. 2020 [internet publication]. [Full text](#)
41. van Doremalen N, Bushmaker T, Morris DH, et al. Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1. *N Engl J Med*. 2020 Apr 16;382(16):1564-7. [Full text](#) [Abstract](#)

42. Guo ZD, Wang ZY, Zhang SF, et al. Aerosol and surface distribution of severe acute respiratory syndrome coronavirus 2 in hospital wards, Wuhan, China, 2020. *Emerg Infect Dis.* 2020 Apr 10;26(7). [Full text](#) [Abstract](#)
43. Zhou J, Otter JA, Price JR, et al. Investigating SARS-CoV-2 surface and air contamination in an acute healthcare setting during the peak of the COVID-19 pandemic in London. *Clin Infect Dis.* 2020 Jul 8 [Epub ahead of print]. [Full text](#) [Abstract](#)
44. van Doorn AS, Meijer B, Frampton CMA, et al. Systematic review with meta-analysis: SARS-CoV-2 stool testing and the potential for faecal-oral transmission. *Aliment Pharmacol Ther.* 2020 Aug 27 [Epub ahead of print]. [Full text](#) [Abstract](#)
45. Zhang W, Du RH, Li B, et al. Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes. *Emerg Microbes Infect.* 2020 Dec;9(1):386-9. [Full text](#) [Abstract](#)
46. To KK, Tsang OT, Chik-Yan Yip C, et al. Consistent detection of 2019 novel coronavirus in saliva. *Clin Infect Dis.* 2020 Jul 28;71(15):841-3. [Full text](#) [Abstract](#)
47. Centre for Evidence-Based Medicine; Ferner RE, Murray PI, Aronson JK. Spreading SARS-CoV-2 through ocular fluids. 2020 [internet publication]. [Full text](#)
48. Sun T, Guan J. Novel coronavirus and central nervous system. *Eur J Neurol.* 2020 Mar 26 [Epub ahead of print]. [Full text](#) [Abstract](#)
49. Seah IYJ, Anderson DE, Kang AEZ, et al. Assessing viral shedding and infectivity of tears in coronavirus disease 2019 (COVID-19) patients. *Ophthalmology.* 2020 Jul;127(7):977-9. [Full text](#) [Abstract](#)
50. Farina A, Uccello G, Spreafico M, et al. SARS-CoV-2 detection in the pericardial fluid of a patient with cardiac tamponade. *Eur J Intern Med.* 2020 Jun;76:100-1. [Full text](#) [Abstract](#)
51. Algarroba GN, Rekawek P, Vahanian SA, et al. Visualization of severe acute respiratory syndrome coronavirus 2 invading the human placenta using electron microscopy. *Am J Obstet Gynecol.* 2020 Aug;223(2):275-8. [Full text](#) [Abstract](#)
52. Li D, Jin M, Bao P, et al. Clinical characteristics and results of semen tests among men with coronavirus disease 2019. *JAMA Netw Open.* 2020 May 1;3(5):e208292. [Full text](#) [Abstract](#)
53. Mei F, Bonifazi M, Menzo S, et al. First detection of SARS-CoV-2 by real-time reverse-transcriptase-polymerase-chain-reaction (RT-PCR) assay in pleural fluid. *Chest.* 2020 Jun 11 [Epub ahead of print]. [Full text](#) [Abstract](#)
54. Kashi AH, De la Rosette J, Amini E, et al. Urinary viral shedding of COVID-19 and its clinical associations: a systematic review and meta-analysis of observational studies. *Urol J.* 2020 Sep 5 [Epub ahead of print]. [Full text](#) [Abstract](#)

55. Frazier KM, Hooper JE, Mostafa HH, et al. SARS-CoV-2 virus isolated from the mastoid and middle ear: implications for COVID-19 precautions during ear surgery. *JAMA Otolaryngol Head Neck Surg*. 2020 Jul 23 [Epub ahead of print]. [Full text](#) [Abstract](#)

---

56. Kotlyar A, Grechukhina O, Chen A, et al. Vertical transmission of COVID-19: a systematic review and meta-analysis. *Am J Obstet Gynecol*. 2020 Jul 30 [Epub ahead of print]. [Full text](#) [Abstract](#)

---

57. Walker KF, O'Donoghue K, Grace N, et al. Maternal transmission of SARS-COV-2 to the neonate, and possible routes for such transmission: a systematic review and critical analysis. *BJOG*. 2020 Jun 12 [Epub ahead of print]. [Full text](#) [Abstract](#)

---

58. Groß R, Conzelmann C, Müller JA, et al. Detection of SARS-CoV-2 in human breastmilk. *Lancet*. 2020 Jun 6;395(10239):1757-8. [Full text](#) [Abstract](#)

---

59. Tam PCK, Ly KM, Kernich ML, et al. Detectable severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in human breast milk of a mildly symptomatic patient with coronavirus disease 2019 (COVID-19). *Clin Infect Dis*. 2020 May 30 [Epub ahead of print]. [Full text](#) [Abstract](#)

---

60. Costa S, Posteraro B, Marchetti S, et al. Excretion of Sars-Cov-2 in human breastmilk samples. *Clin Microbiol Infect*. 2020 Jun 2 [Epub ahead of print]. [Full text](#) [Abstract](#)

---

61. Salvatore CM, Han JY, Acker KP, et al. Neonatal management and outcomes during the COVID-19 pandemic: an observation cohort study. *Lancet Child Adolesc Health*. 2020 Jul 23 [Epub ahead of print]. [Full text](#) [Abstract](#)

---

62. Zhou Q, Gao Y, Wang X, et al. Nosocomial infections among patients with COVID-19, SARS and MERS: a rapid review and meta-analysis. *Ann Transl Med*. 2020 May;8(10):629. [Full text](#) [Abstract](#)

---

63. Rickman HM, Rampling T, Shaw K, et al. Nosocomial transmission of COVID-19: a retrospective study of 66 hospital-acquired cases in a London teaching hospital. *Clin Infect Dis*. 2020 Jun 20 [Epub ahead of print]. [Full text](#) [Abstract](#)

---

64. Rhee C, Baker M, Vaidya V, et al. Incidence of nosocomial COVID-19 in patients hospitalized at a large US academic medical center. *JAMA Netw Open*. 2020 Sep 1;3(9):e2020498. [Full text](#) [Abstract](#)

---

65. Rothe C, Schunk M, Sothmann P, et al. Transmission of 2019-nCoV infection from an asymptomatic contact in Germany. *N Engl J Med*. 2020 Mar 5;382(10):970-71. [Full text](#) [Abstract](#)

---

66. Kupferschmidt K. Study claiming new coronavirus can be transmitted by people without symptoms was flawed. 2020 [internet publication]. [Full text](#)

---

67. Tong ZD, Tang A, Li KF, et al. Potential presymptomatic transmission of SARS-CoV-2, Zhejiang province, China, 2020. *Emerg Infect Dis*. 2020 May 17;26(5). [Full text](#) [Abstract](#)

---

68. Hu Z, Song C, Xu C, et al. Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China. *Sci China Life Sci*. 2020 May;63(5):706-11. [Full text](#) [Abstract](#)

69. Luo SH, Liu W, Liu ZJ, et al. A confirmed asymptomatic carrier of 2019 novel coronavirus (SARS-CoV-2). *Chin Med J (Engl)*. 2020 May 5;133(9):1123-5. [Full text](#) [Abstract](#)
70. Lu S, Lin J, Zhang Z, et al. Alert for non-respiratory symptoms of Coronavirus Disease 2019 (COVID-19) patients in epidemic period: a case report of familial cluster with three asymptomatic COVID-19 patients. *J Med Virol*. 2020 Mar 19 [Epub ahead of print]. [Full text](#) [Abstract](#)
71. Li C, Ji F, Wang L, et al. Asymptomatic and human-to-human transmission of SARS-CoV-2 in a 2-family cluster, Xuzhou, China. *Emerg Infect Dis*. 2020 Mar 31;26(7). [Full text](#) [Abstract](#)
72. Du Z, Xu X, Wu Y, et al. Serial interval of COVID-19 among publicly reported confirmed cases. *Emerg Infect Dis*. 2020 Mar 19;26(6). [Full text](#) [Abstract](#)
73. Wei WE, Li Z, Chiew CJ, et al. Presymptomatic transmission of SARS-CoV-2: Singapore, January 23 - March 16, 2020. *MMWR Morb Mortal Wkly Rep*. 2020 Apr 10;69(14):411-5. [Full text](#) [Abstract](#)
74. Liu J, Huang J, Xiang D. Large SARS-CoV-2 outbreak caused by asymptomatic traveler, China. *Emerg Infect Dis*. 2020 Jun 30;29(9). [Full text](#) [Abstract](#)
75. Jiang XL, Zhang XL, Zhao XN, et al. Transmission potential of asymptomatic and paucisymptomatic severe acute respiratory syndrome coronavirus 2 infections: a three-family cluster study in China. 2020 Jun 11;221(12):1948-52. [Full text](#) [Abstract](#)
76. Luo L, Liu D, Liao X, et al. Contact settings and risk for transmission in 3410 close contacts of patients with COVID-19 in Guangzhou, China: a prospective cohort study. *Ann Intern Med*. 2020 Aug 13 [Epub ahead of print]. [Full text](#) [Abstract](#)
77. World Health Organization. Advice on the use of masks in the context of COVID-19: interim guidance. 2020 [internet publication]. [Full text](#)
78. Gao M, Yang L, Chen X, et al. A study on infectivity of asymptomatic SARS-CoV-2 carriers. *Respir Med*. 2020 May 13;169:106026. [Full text](#) [Abstract](#)
79. Chen F, Fu D, Yang Q, et al. Low transmission risk of 9 asymptomatic carriers tested positive for both SARS-CoV-2 nucleic acid and serum IgG. *J Infect*. 2020 Sep;81(3):452-82. [Full text](#) [Abstract](#)
80. Danis K, Epaulard O, Bénet T, et al. Cluster of coronavirus disease 2019 (Covid-19) in the French Alps, 2020. *Clin Infect Dis*. 2020 Jul 28;71(15):825-32. [Full text](#) [Abstract](#)
81. He J, Guo Y, Mao R, et al. Proportion of asymptomatic coronavirus disease 2019 (COVID-19): a systematic review and meta-analysis. *J Med Virol*. 2020 Jul 21 [Epub ahead of print]. [Full text](#) [Abstract](#)
82. Al-Sadeq DW, Nasrallah GK. The incidence of the novel coronavirus SARS-CoV-2 among asymptomatic patients: a systematic review. *Int J Infect Dis*. 2020 Jul 2;98:372-80. [Full text](#) [Abstract](#)
83. Mizumoto K, Kagaya K, Zarebski A, et al. Estimating the asymptomatic proportion of coronavirus disease 2019 (COVID-19) cases on board the Diamond Princess cruise ship, Yokohama, Japan, 2020. *Euro Surveill*. 2020 Mar;25(10). [Full text](#) [Abstract](#)

84. Day M. Covid-19: identifying and isolating asymptomatic people helped eliminate virus in Italian village. *BMJ*. 2020 Mar 23;368:m1165. [Full text](#) [Abstract](#)
85. Centre for Evidence-Based Medicine; Heneghan C, Brassey J, Jefferson T. COVID-19: What proportion are asymptomatic? 2020 [internet publication]. [Full text](#)
86. Oran DP, Topol EJ. Prevalence of asymptomatic SARS-CoV-2 infection: a narrative review. *Ann Intern Med*. 2020 Jun 3 [Epub ahead of print]. [Full text](#) [Abstract](#)
87. Kimball A, Hatfield KM, Arons M, et al. Asymptomatic and presymptomatic SARS-CoV-2 infections in residents of a long-term care skilled nursing facility: King County, Washington, March 2020. *MMWR Morb Mortal Wkly Rep*. 2020 Apr 3;69(13):377-81. [Full text](#) [Abstract](#)
88. Arons MM, Hatfield KM, Reddy SC, et al. Presymptomatic SARS-CoV-2 infections and transmission in a skilled nursing facility. *N Engl J Med*. 2020 May 28;382(22):2081-90. [Full text](#) [Abstract](#)
89. Stubblefield WB, Talbot HK, Feldstein L, et al. Seroprevalence of SARS-CoV-2 among frontline healthcare personnel during the first month of caring for COVID-19 patients – Nashville, Tennessee. *Clin Infect Dis*. 2020 Jul 6 [Epub ahead of print]. [Full text](#) [Abstract](#)
90. Vahidy FS, Bernard DW, Boom ML, et al. Prevalence of SARS-CoV-2 infection among asymptomatic health care workers in the Greater Houston, Texas, area. *JAMA Netw Open*. 2020 Jul 1;3(7):e2016451. [Full text](#) [Abstract](#)
91. Qiu H, Wu J, Hong L, et al. Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: an observational cohort study. *Lancet Infect Dis*. 2020 Jun;20(6):689-96. [Full text](#) [Abstract](#)
92. Zheng B, Wang H, Yu C. An increasing public health burden arising from children infected with SARS-CoV2: a systematic review and meta-analysis. *Pediatr Pulmonol*. 2020 Aug 5 [Epub ahead of print]. [Full text](#) [Abstract](#)
93. Milani GP, Bottino I, Rocchi A, et al. Frequency of children vs adults carrying severe acute respiratory syndrome coronavirus 2 asymptotically. *JAMA Pediatr*. 2020 Sep 14 [Epub ahead of print]. [Full text](#) [Abstract](#)
94. Frieden TR, Lee CT. Identifying and interrupting superspreading events: implications for control of severe acute respiratory syndrome coronavirus 2. *Emerg Infect Dis*. 2020 Jun;26(6):1059-66. [Full text](#) [Abstract](#)
95. McMichael TM, Clark S, Pogosjans S, et al. COVID-19 in a long-term care facility: King County, Washington, February 27 – March 9, 2020. *MMWR Morb Mortal Wkly Rep*. 2020 Mar 27;69(12):339-42. [Full text](#) [Abstract](#)
96. Moriarty LF, Plucinski MM, Marston BJ, et al. Public health responses to COVID-19 outbreaks on cruise ships: worldwide, February-March 2020. *MMWR Morb Mortal Wkly Rep*. 2020 Mar 27;69(12):347-52. [Full text](#) [Abstract](#)

97. Yang H, Thompson JR. Fighting covid-19 outbreaks in prisons. *BMJ*. 2020 Apr 2;369:m1362. [Full text](#) [Abstract](#)
98. Rogers JH, Link AC, McCulloch D, et al. Characteristics of COVID-19 in homeless shelters: a community-based surveillance study. *Ann Intern Med*. 2020 Sep 15 [Epub ahead of print]. [Full text](#) [Abstract](#)
99. Centre for Evidence-Based Medicine; Durand-Moreau Q, Adisesh A, Mackenzie G, et al. What explains the high rate of SARS-CoV-2 transmission in meat and poultry facilities? 2020 [internet publication]. [Full text](#)
100. Donahue M, Sreenivasan N, Stover D, et al. Notes from the field: characteristics of meat processing facility workers with confirmed SARS-CoV-2 infection – Nebraska, April-May 2020. *MMWR Morb Mortal Wkly Rep*. 2020 Aug 7;69(31):1020-2. [Full text](#) [Abstract](#)
101. Steinberg J, Kennedy ED, Basler C, et al. COVID-19 outbreak among employees at a meat processing facility: South Dakota, March-April 2020. *MMWR Morb Mortal Wkly Rep*. 2020 Aug 7;69(31):1015-9. [Full text](#) [Abstract](#)
102. Heavey L, Casey G, Kelly C, et al. No evidence of secondary transmission of COVID-19 from children attending school in Ireland, 2020. *Euro Surveill*. 2020 May;25(21). [Full text](#) [Abstract](#)
103. Stein RA. Super-spreaders in infectious diseases. *Int J Infect Dis*. 2011 Aug;15(8):e510-3. [Full text](#) [Abstract](#)
104. McAloon C, Collins Á, Hunt K, et al. Incubation period of COVID-19: a rapid systematic review and meta-analysis of observational research. *BMJ Open*. 2020 Aug 16;10(8):e039652. [Full text](#) [Abstract](#)
105. Liu Y, Gayle AA, Wilder-Smith A, et al. The reproductive number of COVID-19 is higher compared to SARS coronavirus. *J Travel Med*. 2020 Mar 13;27(2). [Full text](#) [Abstract](#)
106. Xie Y, Wang Z, Liao H, et al. Epidemiologic, clinical, and laboratory findings of the COVID-19 in the current pandemic: systematic review and meta-analysis. *BMC Infect Dis*. 2020 Aug 31;20(1):640. [Full text](#) [Abstract](#)
107. Centers for Disease Control and Prevention. COVID-19 pandemic planning scenarios. 2020 [internet publication]. [Full text](#)
108. Inglesby TV. Public health measures and the reproduction number of SARS-CoV-2. *JAMA*. 2020 May 1 [Epub ahead of print]. [Full text](#) [Abstract](#)
109. Burke RM, Midgley CM, Dratch A, et al. Active monitoring of persons exposed to patients with confirmed COVID-19 - United States, January-February 2020. *MMWR Morb Mortal Wkly Rep*. 2020 Mar 6;69(9):245-6. [Full text](#) [Abstract](#)
110. Cheng HY, Jian SW, Liu DP, et al. Contact tracing assessment of COVID-19 transmission dynamics in Taiwan and risk at different exposure periods before and after symptom onset. *JAMA Intern Med*. 2020 May 1 [Epub ahead of print]. [Full text](#) [Abstract](#)

111. Wang Z, Ma W, Zheng X, et al. Household transmission of SARS-CoV-2. *J Infect.* 2020 Jul;81(1):179-82. [Full text](#) [Abstract](#)
112. Li W, Zhang B, Lu J, et al. The characteristics of household transmission of COVID-19. *Clin Infect Dis.* 2020 Apr 17 [Epub ahead of print]. [Full text](#) [Abstract](#)
113. Zhang W, Cheng W, Luo L, et al. Secondary transmission of coronavirus disease from presymptomatic persons, China. *Emerg Infect Dis.* 2020 May 26;26(8). [Full text](#) [Abstract](#)
114. Yung CF, Kam KQ, Chong CY, et al. Household transmission of SARS-CoV-2 from adults to children. *J Pediatr.* 2020 Jul 4 [Epub ahead of print]. [Full text](#) [Abstract](#)
115. Macartney K, Quinn HE, Pillsbury AJ, et al. Transmission of SARS-CoV-2 in Australian educational settings: a prospective cohort study. *Lancet Child Adolesc Health.* 2020 Aug 3 [Epub ahead of print]. [Full text](#) [Abstract](#)
116. Ra SH, Lim JS, Kim G, et al. Upper respiratory viral load in asymptomatic individuals and mildly symptomatic patients with SARS-CoV-2 infection. *BMJ Thorax.* 2020 Sep 22 [Epub ahead of print]. [Full text](#)
117. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet.* 2020 Mar 28;395(10229):1054-62. [Full text](#) [Abstract](#)
118. Chang, Mo G, Yuan X, et al. Time kinetics of viral clearance and resolution of symptoms in novel coronavirus infection. *Am J Respir Crit Care Med.* 2020 May 1;201(9):1150-2. [Full text](#) [Abstract](#)
119. Yang JR, Deng DT, Wu N, et al. Persistent viral RNA positivity during recovery period of a patient with SARS-CoV-2 infection. *J Med Virol.* 2020 Apr 24 [Epub ahead of print]. [Abstract](#)
120. Jiang X, Luo M, Zou Z, et al. Asymptomatic SARS-CoV-2 infected case with viral detection positive in stool but negative in nasopharyngeal samples lasts for 42 days. *J Med Virol.* 2020 Apr 24 [Epub ahead of print]. [Abstract](#)
121. Li J, Zhang L, Liu B, et al. Case report: viral shedding for 60 days in a woman with novel coronavirus disease (COVID-19). *Am J Trop Med Hyg.* 2020 Jun;102(6):1210-3. [Full text](#) [Abstract](#)
122. Sun J, Xiao J, Sun R, et al. Prolonged persistence of SARS-CoV-2 RNA in body fluids. *Emerg Infect Dis.* 2020 May 8;26(8). [Full text](#) [Abstract](#)
123. Molina LP, Chow SK, Nickel A, et al. Prolonged detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA in an obstetric patient with antibody seroconversion. *Obstet Gynecol.* 2020 Jul 21 [Epub ahead of print]. [Full text](#) [Abstract](#)
124. Noh JY, Yoon JG, Seong H, et al. Asymptomatic infection and atypical manifestations of COVID-19: comparison of viral shedding duration. *J Infect.* 2020 May 20 [Epub ahead of print]. [Full text](#) [Abstract](#)

125. Zheng S, Fan J, Yu F, et al. Viral load dynamics and disease severity in patients infected with SARS-CoV-2 in Zhejiang province, China, January – March 2020: retrospective cohort study. *BMJ*. 2020 Apr 21;369:m1443. [Full text](#) [Abstract](#)
126. Widders A, Broom A, Broom J. SARS-CoV-2: the viral shedding vs infectivity dilemma. *Infect Dis Health*. 2020 Aug;25(3):210-5. [Full text](#) [Abstract](#)
127. Xu K, Chen Y, Yuan J, et al. Factors associated with prolonged viral RNA shedding in patients with COVID-19. *Clin Infect Dis*. 2020 Jul 28;71(15):799-806. [Full text](#) [Abstract](#)
128. Yan R, Zhang Y, Li Y, et al. Structural basis for the recognition of the SARS-CoV-2 by full-length human ACE2. *Science*. 2020 Mar 27;367(6485):1444-8. [Full text](#) [Abstract](#)
129. Chen Y, Guo Y, Pan Y, et al. Structure analysis of the receptor binding of 2019-nCoV. *Biochem Biophys Res Commun*. 2020 Feb 17;525(1):135-40. [Full text](#) [Abstract](#)
130. Hanff TC, Harhay MO, Brown TS, et al. Is there an association between COVID-19 mortality and the renin-angiotensin system: a call for epidemiologic investigations. *Clin Infect Dis*. 2020 Jul 28;71(15):870-4. [Full text](#) [Abstract](#)
131. Wu Z, Hu R, Zhang C, et al. Elevation of plasma angiotensin II level is a potential pathogenesis for the critically ill COVID-19 patients. *Crit Care*. 2020 Jun 5;24(1):290. [Full text](#) [Abstract](#)
132. Zou X, Chen K, Zou J, et al. Single-cell RNA-seq data analysis on the receptor ACE2 expression reveals the potential risk of different human organs vulnerable to 2019-nCoV infection. *Front Med*. 2020 Apr;14(2):185-92. [Full text](#) [Abstract](#)
133. Bunyavanich S, Do A, Vicencio A. Nasal gene expression of angiotensin-converting enzyme 2 in children and adults. *JAMA*. 2020 May 20;323(23):2427-9. [Full text](#) [Abstract](#)
134. Hoffmann M, Kleine-Weber H, Schroeder S, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. *Cell*. 2020 Apr 16;181(2):271-80. [Full text](#) [Abstract](#)
135. Bunyavanich S, Grant C, Vicencio A. Racial/ethnic variation in nasal gene expression of transmembrane serine protease 2 (TMPRSS2). *JAMA*. 2020 Sep 10 [Epub ahead of print]. [Full text](#) [Abstract](#)
136. Coutard B, Valle C, de Lamballerie X, et al. The spike glycoprotein of the new coronavirus 2019-nCoV contains a furin-like cleavage site absent in CoV of the same clade. *Antiviral Res*. 2020 Feb 10;176:104742. [Abstract](#)
137. Menter T, Haslbauer JD, Nienhold R, et al. Post-mortem examination of COVID19 patients reveals diffuse alveolar damage with severe capillary congestion and variegated findings of lungs and other organs suggesting vascular dysfunction. *Histopathology*. 2020 May 4 [Epub ahead of print]. [Full text](#) [Abstract](#)
138. Schaller T, Hirschtbühl K, Burkhardt K, et al. Postmortem examination of patients with COVID-19. *JAMA*. 2020 May 21;323(24):2518-20. [Full text](#) [Abstract](#)

139. Lax SF, Skok K, Zechner P, et al. Pulmonary arterial thrombosis in COVID-19 with fatal outcome: results from a prospective, single-center, clinicopathologic case series. *Ann Intern Med*. 2020 May 14 [Epub ahead of print]. [Full text](#) [Abstract](#)
140. Ackermann M, Verleden SE, Kuehnel M, et al. Pulmonary vascular endothelialitis, thrombosis, and angiogenesis in Covid-19. *N Engl J Med*. 2020 Jul 9;383(2):120-8. [Full text](#) [Abstract](#)
141. Fox SE, Akmatbekov A, Harbert JL, et al. Pulmonary and cardiac pathology in African American patients with COVID-19: an autopsy series from New Orleans. *Lancet Respir Med*. 2020 Jul;8(7):681-6. [Full text](#) [Abstract](#)
142. Carsana L, Sonzogni A, Nasr A, et al. Pulmonary post-mortem findings in a series of COVID-19 cases from northern Italy: a two-centre descriptive study. *Lancet Infect Dis*. 2020 Jun 8 [Epub ahead of print]. [Full text](#) [Abstract](#)
143. Solomon IH, Normandin E, Bhattacharyya S, et al. Neuropathological features of Covid-19. *N Engl J Med*. 2020 Jun 12 [Epub ahead of print]. [Full text](#) [Abstract](#)
144. Lindner D, Fitzek A, Bräuninger H, et al. Association of cardiac infection with SARS-CoV-2 in confirmed COVID-19 autopsy cases. *JAMA Cardiol*. 2020 Jul 27 [Epub ahead of print]. [Full text](#) [Abstract](#)
145. Dolhnikoff M, Ferreira Ferranti J, de Almeida Monteiro RA, et al. SARS-CoV-2 in cardiac tissue of a child with COVID-19-related multisystem inflammatory syndrome. *Lancet Child Adolesc Health*. 2020 Aug 20 [Epub ahead of print]. [Full text](#) [Abstract](#)
146. Hanley B, Naresh KN, Roufousse C, et al. Histopathological findings and viral tropism in UK patients with severe fatal COVID-19: a post-mortem study. *Lancet Microbe*. 2020 Aug 20 [Epub ahead of print]. [Full text](#) [Abstract](#)
147. Sardu C, Gambardella J, Morelli MB, et al. Hypertension, thrombosis, kidney failure, and diabetes: is COVID-19 an endothelial disease? A comprehensive evaluation of clinical and basic evidence. *J Clin Med*. 2020 May 11;9(5): E1417. [Full text](#) [Abstract](#)
148. Tibiriçá E, De Lorenzo A. Increased severity of COVID-19 in people with obesity: are we overlooking plausible biological mechanisms? *Obesity (Silver Spring)*. 2020 May 13 [Epub ahead of print]. [Full text](#) [Abstract](#)
149. Bermejo-Martin JF, Almansa R, Torres A, et al. COVID-19 as a cardiovascular disease: the potential role of chronic endothelial dysfunction. *Cardiovasc Res*. 2020 Aug 1;116(10):e132-3. [Full text](#) [Abstract](#)
150. Goshua G, Pine AB, Meizlish ML, et al. Endotheliopathy in COVID-19-associated coagulopathy: evidence from a single-centre, cross-sectional study. *Lancet Haematol*. 2020 Aug;7(8):e575-82. [Full text](#) [Abstract](#)
151. Maier CL, Truong AD, Auld SC, et al. COVID-19-associated hyperviscosity: a link between inflammation and thrombophilia? *Lancet*. 2020 Jun 6;395(10239):1758-9. [Full text](#) [Abstract](#)

152. van der Made CI, Simons A, Schuurs-Hoeijmakers J, et al. Presence of genetic variants among young men with severe COVID-19. *JAMA*. 2020 Jul 24;324(7):1-11. [Full text](#) [Abstract](#)
153. World Health Organization. Public health surveillance for COVID-19: interim guidance. 2020 [internet publication]. [Full text](#)
154. Shen N, Zhu Y, Wang X, et al. Characteristics and diagnosis rate of 5,630 subjects receiving SARS-CoV-2 nucleic acid tests from Wuhan, China. *JCI Insight*. 2020 May 21;5(10):e137662. [Full text](#) [Abstract](#)
155. de Lusignan S, Dorward J, Correa A, et al. Risk factors for SARS-CoV-2 among patients in the Oxford Royal College of General Practitioners Research and Surveillance Centre primary care network: a cross-sectional study. *Lancet Infect Dis*. 2020 May 15 [Epub ahead of print]. [Full text](#) [Abstract](#)
156. Centers for Disease Control and Prevention. Coronavirus disease 2019 (COVID-19): older adults. 2020 [internet publication]. [Full text](#)
157. Centers for Disease Control and Prevention. Coronavirus disease 2019 (COVID-19): people who are at higher risk for severe illness. 2020 [internet publication]. [Full text](#)
158. Bonanad C, García-Blas S, Tarazona-Santabalbina F, et al. The effect of age on mortality in patients with COVID-19: a meta-analysis with 611,583 subjects. *J Am Med Dir Assoc*. 2020 Jul;21(7):915-8. [Full text](#) [Abstract](#)
159. Burki T. England and Wales see 20 000 excess deaths in care homes. *Lancet*. 2020 May 23;395(10237):1602. [Full text](#) [Abstract](#)
160. Iacobucci G. Covid-19: Nearly half of care homes in northeast England have had an outbreak. *BMJ*. 2020 May 20;369:m2041. [Full text](#) [Abstract](#)
161. Graham N, Junghans C, Downes R, et al. SARS-CoV-2 infection, clinical features and outcome of COVID-19 in United Kingdom nursing homes. *J Infect*. 2020 Sep;81(3):411-9. [Full text](#) [Abstract](#)
162. Ortolan A, Lorenzin M, Felicetti M, et al. Does gender influence clinical expression and disease outcomes in COVID-19? A systematic review and meta-analysis. *Int J Infect Dis*. 2020 Aug 12 [Epub ahead of print]. [Full text](#) [Abstract](#)
163. Montopoli M, Zumerle S, Vettor R, et al. Androgen-deprivation therapies for prostate cancer and risk of infection by SARS-CoV-2: a population-based study (n=4532). *Ann Oncol*. 2020 Aug;31(8):1040-5. [Full text](#) [Abstract](#)
164. Zeng F, Dai C, Cai P, et al. A comparison study of SARS-CoV-2 IgG antibody between male and female COVID-19 patients: a possible reason underlying different outcome between sex. *J Med Virol*. 2020 May 8 [Epub ahead of print]. [Full text](#) [Abstract](#)
165. Takahashi T, Ellingson MK, Wong P, et al. Sex differences in immune responses that underlie COVID-19 disease outcomes. *Nature*. 2020 Aug 19 [Epub ahead of print]. [Full text](#)
166. Raisi-Estabragh Z, McCracken C, Bethell MS, et al. Greater risk of severe COVID-19 in Black, Asian and Minority Ethnic populations is not explained by cardiometabolic, socioeconomic or behavioural

- factors, or by 25(OH)-vitamin D status: study of 1326 cases from the UK Biobank. *J Public Health (Oxf)*. 2020 Aug 18;42(3):451-60. [Full text](#) [Abstract](#)
167. Hull SA, Williams C, Ashworth M, et al. Prevalence of suspected COVID-19 infection in patients from ethnic minority populations: a cross-sectional study in primary care. *Br J Gen Pract*. 2020 Sep 7 [Epub ahead of print]. [Full text](#) [Abstract](#)
168. Alaa AM, Qian Z, Rashbass J, et al. Ethnicity and outcomes of COVID-19 patients in England. 2020 [internet publication]. [Full text](#)
169. Harrison EM, Docherty AB, Barr B, et al; SSRN. Ethnicity and outcomes from COVID-19: the ISARIC CCP-UK prospective observational cohort study of hospitalised patients. 2020 [internet publication]. [Full text](#)
170. Centers for Disease Control and Prevention. COVID-19 in racial and ethnic minority groups. 2020 [internet publication]. [Full text](#)
171. Yehia BR, Winegar A, Fogel R, et al. Association of race with mortality among patients hospitalized with coronavirus disease 2019 (COVID-19) at 92 US hospitals. *JAMA Netw Open*. 2020 Aug 3;3(8):e2018039. [Full text](#) [Abstract](#)
172. Wortham JM, Lee JT, Althomsons S, et al. Characteristics of persons who died with COVID-19: United States, February 12 – May 18, 2020. *MMWR Morb Mortal Wkly Rep*. 2020 Jul 17;69(28):923-9. [Full text](#) [Abstract](#)
173. Liu H, Chen S, Liu M, et al. Comorbid chronic diseases are strongly correlated with disease severity among COVID-19 patients: a systematic review and meta-analysis. *Aging Dis*. 2020 May 9;11(3):668-78. [Full text](#) [Abstract](#)
174. Centers for Disease Control and Prevention. Coronavirus disease 2019 (COVID-19): people with certain medical conditions. 2020 [internet publication]. [Full text](#)
175. Centers for Disease Control and Prevention. COVIDView: a weekly surveillance summary of US COVID-19 activity. 2020 [internet publication]. [Full text](#)
176. Mahumud RA, Kamara JK, Renzaho AMN. The epidemiological burden of and overall distribution of chronic comorbidities in coronavirus disease-2019 among 202,005 infected patients: evidence from a systematic review and meta-analysis. *Infection*. 2020 Aug 19;1-21. [Full text](#) [Abstract](#)
177. Stokes EK, Zambrano LD, Anderson KN, et al. Coronavirus disease 2019 case surveillance: United States, January 22–May 30, 2020. *MMWR Morb Mortal Wkly Rep*. 2020 Jun 19;69(24):759-65. [Full text](#) [Abstract](#)
178. Adams ML, Katz DL, Grandpre J. Updated estimates of chronic conditions affecting risk for complications from coronavirus disease, United States. *Emerg Infect Dis*. 2020 Jul 3;26(9). [Full text](#) [Abstract](#)
179. CDC COVID-19 Response Team. Coronavirus disease 2019 in children: United States, February 12 - April 2, 2020. *MMWR Morb Mortal Wkly Rep*. 2020 Apr 10;69(14):422-6. [Full text](#) [Abstract](#)

180. DeBiasi RL, Song X, Delaney M, et al. Severe COVID-19 in children and young adults in the Washington, DC metropolitan region. *J Pediatr*. 2020 Aug;223:199-203. [Full text](#) [Abstract](#)
181. Adams SH, Park MJ, Schaub JP, et al. Medical vulnerability of young adults to severe COVID-19 illness: data from the National Health Interview Survey. *J Adolesc Health*. 2020 Jul 9;67(3):362-8. [Full text](#) [Abstract](#)
182. Aggarwal G, Cheruiyot I, Aggarwal S, et al. Association of cardiovascular disease with coronavirus disease 2019 (COVID-19) severity: a meta-analysis. *Curr Probl Cardiol*. 2020 Apr 28:100617. [Full text](#) [Abstract](#)
183. Pranata R, Lim MA, Huang I, et al. Hypertension is associated with increased mortality and severity of disease in COVID-19 pneumonia: a systematic review, meta-analysis and meta-regression. *J Renin Angiotensin Aldosterone Syst*. 2020 Apr-Jun;21(2):1470320320926899. [Full text](#) [Abstract](#)
184. Zhang J, Wu J, Sun X, et al. Associations of hypertension with the severity and fatality of SARS-CoV-2 infection: a meta-analysis. *Epidemiol Infect*. 2020 May 28;:1-19. [Abstract](#)
185. Hussain S, Baxi H, Chand Jamali M, et al. Burden of diabetes mellitus and its impact on COVID-19 patients: a meta-analysis of real-world evidence. *Diabetes Metab Syndr*. 2020 Aug 20;14(6):1595-602. [Full text](#) [Abstract](#)
186. Huang I, Lim MA, Pranata R. Diabetes mellitus is associated with increased mortality and severity of disease in COVID-19 pneumonia: a systematic review, meta-analysis, and meta-regression. *Diabetes Metab Syndr*. 2020 Apr 17;14(4):395-403. [Full text](#) [Abstract](#)
187. Seigle J, Platt J, Cromer SJ, et al. Diabetes as a risk factor for poor early outcomes in patients hospitalized with COVID-19. *Diabetes Care*. 2020 Aug 26 [Epub ahead of print]. [Full text](#) [Abstract](#)
188. Chen Y, Yang D, Cheng B, et al. Clinical characteristics and outcomes of patients with diabetes and COVID-19 in association with glucose-lowering medication. *Diabetes Care*. 2020 Jul;43(7):1399-407. [Full text](#) [Abstract](#)
189. Holman N, Knighton P, Kar P, et al. Risk factors for COVID-19-related mortality in people with type 1 and type 2 diabetes in England: a population-based cohort study. *Lancet Diabetes Endocrinol*. 2020 Aug 13 [Epub ahead of print]. [Full text](#) [Abstract](#)
190. Pal R, Banerjee M, Yadav U, et al. Clinical profile and outcomes in COVID-19 patients with diabetic ketoacidosis: a systematic review of literature. *Diabetes Metab Syndr*. 2020 Aug 18;14(6):1563-9. [Full text](#) [Abstract](#)
191. Agarwal S, Schechter C, Southern W, et al. Preadmission diabetes-specific risk factors for mortality in hospitalized patients with diabetes and coronavirus disease 2019. *Diabetes Care*. 2020 Aug 7 [Epub ahead of print]. [Full text](#) [Abstract](#)
192. Coppelli A, Giannarelli R, Aragona M, et al. Hyperglycemia at hospital admission is associated with severity of the prognosis in patients hospitalized for COVID-19: the Pisa COVID-19 study. *Diabetes Care*. 2020 Aug 11 [Epub ahead of print]. [Full text](#) [Abstract](#)

193. Lee MH, Wong C, Ng CH, et al. Effects of hyperglycaemia on complications of COVID-19: a meta-analysis of observational studies. *Diabetes Obes Metab.* 2020 Sep 1 [Epub ahead of print]. [Full text](#) [Abstract](#)
194. Barron E, Bakhai C, Kar P, et al. Associations of type 1 and type 2 diabetes with COVID-19-related mortality in England: a whole-population study. *Lancet Diabetes Endocrinol.* 2020 Aug 13 [Epub ahead of print]. [Full text](#) [Abstract](#)
195. Li H, Tian S, Chen T, et al. Newly diagnosed diabetes is associated with a higher risk of mortality than known diabetes in hospitalized patients with COVID-19. *Diabetes Obes Metab.* 2020 May 29 [Epub ahead of print]. [Full text](#) [Abstract](#)
196. Apicella M, Campopiano MC, Mantuano M, et al. COVID-19 in people with diabetes: understanding the reasons for worse outcomes. *Lancet Diabetes Endocrinol.* 2020 Sep;8(9):782-92. [Full text](#) [Abstract](#)
197. Halpin DMG, Faner R, Sibila O, et al. Do chronic respiratory diseases or their treatment affect the risk of SARS-CoV-2 infection? *Lancet Respir Med.* 2020 May;8(5):436-8. [Full text](#) [Abstract](#)
198. Centre for Evidence-Based Medicine; Hartmann-Boyce J, Otunla A, Drake J, et al. Asthma and COVID-19: risks and management considerations. 2020 [internet publication]. [Full text](#)
199. Lippi G, Henry BM. Chronic obstructive pulmonary disease is associated with severe coronavirus disease 2019 (COVID-19). *Respir Med.* 2020 Jun;167:105941. [Full text](#) [Abstract](#)
200. Wang Y, Chen J, Chen W, et al. Does asthma increase the mortality of patients with COVID-19? A systematic review and meta-analysis. *Int Arch Allergy Immunol.* 2020 Sep 22;:1-7. [Full text](#) [Abstract](#)
201. Broadhurst R, Peterson R, Wisnivesky JP, et al. Asthma in COVID-19 hospitalizations: an overestimated risk factor? *Ann Am Thorac Soc.* 2020 Aug 31 [Epub ahead of print]. [Full text](#) [Abstract](#)
202. Castro-Rodriguez JA, Forno E. Asthma and COVID-19 in children: a systematic review and call for data. *Pediatr Pulmonol.* 2020 Jun 18 [Epub ahead of print]. [Full text](#) [Abstract](#)
203. Kunutsor SK, Laukkanen JA. Renal complications in COVID-19: a systematic review and meta-analysis. *Ann Med.* 2020 Jul 10;:1-9. [Full text](#) [Abstract](#)
204. Yu J Ouyang W, Chua ML, et al. SARS-CoV-2 transmission in patients with cancer at a tertiary care hospital in Wuhan, China. *JAMA Oncol.* 2020 Mar 25;6(7):1108-10. [Full text](#) [Abstract](#)
205. Tian Y, Qiu X, Wang C, et al. Cancer associates with risk and severe events of COVID-19: a systematic review and meta-analysis. *Int J Cancer.* 2020 Jul 19 [Epub ahead of print]. [Full text](#) [Abstract](#)
206. Ofori-Asenso R, Ogundipe O, Agyeman AA, et al. Cancer is associated with severe disease in COVID-19 patients: a systematic review and meta-analysis. *Ecancermedicallscience.* 2020 May 18;14:1047. [Full text](#) [Abstract](#)

207. Tian J, Yuan X, Xiao J, et al. Clinical characteristics and risk factors associated with COVID-19 disease severity in patients with cancer in Wuhan, China: a multicentre, retrospective, cohort study. *Lancet Oncol*. 2020 May 29;21(7):893-903. [Full text](#) [Abstract](#)
208. Giannakoulis VG, Papoutsis E, Siempos II. Effect of cancer on clinical outcomes of patients with COVID-19: a meta-analysis of patient data. *JCO Glob Oncol*. 2020 Jun;6:799-808. [Full text](#) [Abstract](#)
209. Passamonti F, Cattaneo C, Arcaini L, et al. Clinical characteristics and risk factors associated with COVID-19 severity in patients with haematological malignancies in Italy: a retrospective, multicentre, cohort study. *Lancet Haematol*. 2020 Aug 13 [Epub ahead of print]. [Full text](#) [Abstract](#)
210. Lee LYW, Cazier JB, Starkey T, et al. COVID-19 prevalence and mortality in patients with cancer and the effect of primary tumour subtype and patient demographics: a prospective cohort study. *Lancet Oncol*. 2020 Aug 24 [Epub ahead of print]. [Full text](#) [Abstract](#)
211. Salunke AA, Nandy K, Pathak SK, et al. Impact of COVID -19 in cancer patients on severity of disease and fatal outcomes: a systematic review and meta-analysis. *Diabetes Metab Syndr*. 2020 Jul 28;14(5):1431-7. [Full text](#) [Abstract](#)
212. Dai M, Liu D, Liu M, et al. Patients with cancer appear more vulnerable to SARS-COV-2: a multi-center study during the COVID-19 outbreak. *Cancer Discov*. 2020 Jun;10(6):783-91. [Full text](#) [Abstract](#)
213. Kuderer NM, Choueiri TK, Shah DP, et al. Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. *Lancet*. 2020 Jun 20;395(10241):1907-18. [Full text](#) [Abstract](#)
214. Lee LYW, Cazier JB, Starkey T, et al. COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: a prospective cohort study. *Lancet*. 2020 Jun 20;395(10241):1919-26. [Full text](#) [Abstract](#)
215. Yang K, Sheng Y, Huang C, et al. Clinical characteristics, outcomes, and risk factors for mortality in patients with cancer and COVID-19 in Hubei, China: a multicentre, retrospective, cohort study. *Lancet Oncol*. 2020 May 29;21(7):904-13. [Full text](#) [Abstract](#)
216. Boulad F, Kamboj M, Bouvier N, et al. COVID-19 in children with cancer in New York City. *JAMA Oncol*. 2020 May 13 [Epub ahead of print]. [Full text](#) [Abstract](#)
217. Afshar ZM, Dayani M, Naderi M, et al. Fatality rate of COVID-19 in patients with malignancies: a systematic review and meta-analysis. *J Infect*. 2020 Aug;81(2):e114-6. [Full text](#) [Abstract](#)
218. Popkin BM, Du S, Green WD, et al. Individuals with obesity and COVID-19: a global perspective on the epidemiology and biological relationships. *Obes Rev*. 2020 Aug 26 [Epub ahead of print]. [Full text](#) [Abstract](#)
219. Du Y, Lv Y, Zha W, et al. Association of body mass index (BMI) with critical COVID-19 and in-hospital mortality: a dose-response meta-analysis. *Metabolism*. 2020 Sep 16:154373. [Full text](#) [Abstract](#)
220. Tartof SY, Qian L, Hong V, et al. Obesity and mortality among patients diagnosed with COVID-19: results from an integrated health care organization. *Ann Intern Med*. 2020 Aug 12 [Epub ahead of print]. [Full text](#) [Abstract](#)

221. Savasi VM, Parisi F, Patanè L, et al. Clinical findings and disease severity in hospitalized pregnant women with coronavirus disease 2019 (COVID-19). *Obstet Gynecol*. 2020 Aug;136(2):252-8. [Full text](#) [Abstract](#)
222. Zachariah P, Johnson CL, Halabi KC, et al. Epidemiology, clinical features, and disease severity in patients with coronavirus disease 2019 (COVID-19) in a children's hospital in New York City, New York. *JAMA Pediatr*. 2020 Jun 3:e202430. [Full text](#) [Abstract](#)
223. Panepinto JA, Brandow A, Mucalo L, et al. Coronavirus disease among persons with sickle cell disease, United States, March 20 – May 21, 2020. *Emerg Infect Dis*. 2020 Jul 8;26(10). [Full text](#) [Abstract](#)
224. Hussain FA, Njoku FU, Saraf SL, et al. COVID-19 infection in patients with sickle cell disease. *Br J Haematol*. 2020 Jun;189(5):851-2. [Full text](#) [Abstract](#)
225. Nur E, Gaartman AE, van Tuijn CFJ, et al. Vaso-occlusive crisis and acute chest syndrome in sickle cell disease due to 2019 novel coronavirus disease (COVID-19). *Am J Hematol*. 2020 Jun;95(6):725-6. [Full text](#) [Abstract](#)
226. Pereira MR, Mohan S, Cohen DJ, et al. COVID-19 in solid organ transplant recipients: initial report from the US epicenter. *Am J Transplant*. 2020 Jul;20(7):1800-8. [Full text](#) [Abstract](#)
227. Zhu L, Gong N, Liu B, et al. Coronavirus disease 2019 pneumonia in immunosuppressed renal transplant recipients: a summary of 10 confirmed cases in Wuhan, China. *Eur Urol*. 2020 Jun;77(6):748-54. [Full text](#) [Abstract](#)
228. Akalin E, Azzi Y, Bartash R, et al. Covid-19 and kidney transplantation. *N Engl J Med*. 2020 Jun 18;382(25):2475-7. [Full text](#) [Abstract](#)
229. Columbia University Kidney Transplant Program. Early description of coronavirus 2019 disease in kidney transplant recipients in New York. *J Am Soc Nephrol*. 2020 Jun;31(6):1150-6. [Full text](#) [Abstract](#)
230. Banerjee D, Popoola J, Shah S, et al. COVID-19 infection in kidney transplant recipients. *Kidney Int*. 2020 Jun;97(6):1076-82. [Full text](#) [Abstract](#)
231. Latif F, Farr MA, Clerkin KJ, et al. Characteristics and outcomes of recipients of heart transplant with coronavirus disease 2019. *JAMA Cardiol*. 2020 May 13 [Epub ahead of print]. [Full text](#) [Abstract](#)
232. Fraser J, Mousley J, Testro A, et al. Clinical presentation, treatment, and mortality rate in liver transplant recipients with coronavirus disease 2019: a systematic review and quantitative analysis. *Transplant Proc*. 2020 Jul 30 [Epub ahead of print]. [Full text](#) [Abstract](#)
233. Reddy RK, Charles WN, Sklavounos A, et al. The effect of smoking on COVID-19 severity: a systematic review and meta-analysis. *J Med Virol*. 2020 Aug 4 [Epub ahead of print]. [Full text](#) [Abstract](#)
234. Cai G, Bossé Y, Xiao F, et al. Tobacco smoking increases the lung gene expression of ACE2, the receptor of SARS-CoV-2. *Am J Respir Crit Care Med*. 2020 Jun 15;201(12):1557-9. [Full text](#) [Abstract](#)

235. World Health Organization. Smoking and COVID-19: scientific brief. 2020 [internet publication]. [Full text](#)
236. Patel U, Malik P, Shah D, et al. Pre-existing cerebrovascular disease and poor outcomes of COVID-19 hospitalized patients: a meta-analysis. *J Neurol*. 2020 Aug 8 [Epub ahead of print]. [Full text](#) [Abstract](#)
237. Kovalic AJ, Satapathy SK, Thuluvath PJ. Prevalence of chronic liver disease in patients with COVID-19 and their clinical outcomes: a systematic review and meta-analysis. *Hepatol Int*. 2020 Jul 28 [Epub ahead of print]. [Full text](#) [Abstract](#)
238. Iavarone M, D'Ambrosio R, Soria A, et al. High rates of 30-day mortality in patients with cirrhosis and COVID-19. *J Hepatol*. 2020 Jun 8 [Epub ahead of print]. [Full text](#) [Abstract](#)
239. Hariyanto TI, Kurniawan A. Dyslipidemia is associated with severe coronavirus disease 2019 (COVID-19) infection. *Diabetes Metab Syndr*. 2020 Aug 1;14(5):1463-5. [Full text](#) [Abstract](#)
240. Ji D, Qin E, Xu J, et al. Non-alcoholic fatty liver diseases in patients with COVID-19: a retrospective study. *J Hepatol*. 2020 Apr 8;73(2):451-3. [Full text](#) [Abstract](#)
241. Sharma P, Kumar A. Metabolic dysfunction associated fatty liver disease increases risk of severe Covid-19. *Diabetes Metab Syndr*. 2020 Jun 10;14(5):825-7. [Full text](#) [Abstract](#)
242. Targher G, Mantovani A, Byrne CD, et al. Risk of severe illness from COVID-19 in patients with metabolic dysfunction-associated fatty liver disease and increased fibrosis scores. *Gut*. 2020 Aug;69(8):1545-7. [Full text](#) [Abstract](#)
243. Zhou YJ, Zheng KI, Wang XB, et al. Younger patients with MAFLD are at increased risk of severe COVID-19 illness: a multicenter preliminary analysis. *J Hepatol*. 2020 Sep;73(3):719-21. [Full text](#) [Abstract](#)
244. Doglietto F, Vezzoli M, Gheza F, et al. Factors associated with surgical mortality and complications among patients with and without coronavirus disease 2019 (COVID-19) in Italy. *JAMA Surg*. 2020 Jun 12 [Epub ahead of print]. [Full text](#) [Abstract](#)
245. Lei S, Jiang F, Su W, et al. Clinical characteristics and outcomes of patients undergoing surgeries during the incubation period of COVID-19 infection. *EClinicalMedicine*. 2020 Apr 5:100331. [Full text](#) [Abstract](#)
246. COVIDSurg Collaborative. Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study. *Lancet*. 2020 Jul 4;396(10243):27-38. [Full text](#) [Abstract](#)
247. Singh S, Khan A, Chowdhry M, et al. Risk of severe COVID-19 in patients with inflammatory bowel disease in United States: a multicenter research network study. *Gastroenterology*. 2020 Jun 6 [Epub ahead of print]. [Full text](#) [Abstract](#)
248. Gianfrancesco M, Hyrich KL, Al-Adely S, et al. Characteristics associated with hospitalisation for COVID-19 in people with rheumatic disease: data from the COVID-19 Global Rheumatology Alliance physician-reported registry. *Ann Rheum Dis*. 2020 Jul;79(7):859-66. [Full text](#) [Abstract](#)

249. Centre for Evidence-Based Medicine; Hoang U, Jones NR. Is there an association between exposure to air pollution and severity of COVID-19 infection? 2020 [internet publication]. [Full text](#)
250. Copat C, Cristaldi A, Fiore M, et al. The role of air pollution (PM and NO<sub>2</sub>) in COVID-19 spread and lethality: a systematic review. *Environ Res*. 2020 Aug 24;191:110129. [Full text](#) [Abstract](#)
251. Frontera A, Cianfanelli L, Vlachos K, et al. Severe air pollution links to higher mortality in COVID-19 patients: the “double-hit” hypothesis. *J Infect*. 2020 Aug;81(2):255-9. [Full text](#) [Abstract](#)
252. Ogen Y. Assessing nitrogen dioxide (NO<sub>2</sub>) levels as a contributing factor to coronavirus (COVID-19) fatality. *Sci Total Environ*. 2020 Apr 11;726:138605. [Full text](#) [Abstract](#)
253. Wu X, Nethery RC, Sabath BM, et al; medRxiv. Exposure to air pollution and COVID-19 mortality in the United States: a nationwide cross-sectional study. 2020 [internet publication]. [Full text](#)
254. Sajadi MM, Habibzadeh P, Vintzileos A, et al. Temperature, humidity, and latitude analysis to estimate potential spread and seasonality of coronavirus disease 2019 (COVID-19). *JAMA Netw Open*. 2020 Jun 1;3(6):e2011834. [Full text](#) [Abstract](#)
255. Centre for Evidence-Based Medicine; Spencer EA, Brassey J, Jefferson T, et al. Environmental weather conditions and influence on transmission of SARS-CoV-2. 2020 [internet publication]. [Full text](#)
256. Mecenas P, Bastos RTDRM, Vallinoto ACR, et al. Effects of temperature and humidity on the spread of COVID-19: a systematic review. *PLoS One*. 2020;15(9):e0238339. [Full text](#) [Abstract](#)
257. Yao Y, Pan J, Liu Z, et al. No association of COVID-19 transmission with temperature or UV radiation in Chinese cities. *Eur Respir J*. 2020 May 7;55(5):2000517. [Full text](#) [Abstract](#)
258. Baker RE, Yang W, Vecchi GA, et al. Susceptible supply limits the role of climate in the early SARS-CoV-2 pandemic. *Science*. 2020 Jul 17;369(6501):315-9. [Full text](#) [Abstract](#)
259. Sehra ST, Saliccioli JD, Wiebe DJ, et al. Maximum daily temperature, precipitation, ultra-violet light and rates of transmission of SARS-Cov-2 in the United States. *Clin Infect Dis*. 2020 May 30 [Epub ahead of print]. [Full text](#) [Abstract](#)
260. Centre for Evidence-Based Medicine; Heneghan C, Jefferson T. Effect of latitude on COVID-19. 2020 [internet publication]. [Full text](#)
261. Whittemore PB. COVID-19 fatalities, latitude, sunlight, and vitamin D. *Am J Infect Control*. 2020 Jun 26 [Epub ahead of print]. [Full text](#) [Abstract](#)
262. Meltzer DO, Best TJ, Zhang H, et al. Association of vitamin D status and other clinical characteristics with COVID-19 test results. *JAMA Netw Open*. 2020 Sep 1;3(9):e2019722. [Full text](#) [Abstract](#)
263. Merzon E, Tworowski D, Gorohovski A, et al. Low plasma 25(OH) vitamin D level is associated with increased risk of COVID-19 infection: an Israeli population-based study. *FEBS J*. 2020 Jul 23 [Epub ahead of print]. [Full text](#) [Abstract](#)

264. Lau FH, Majumder R, Torabi R, et al; medRxiv. Vitamin D insufficiency is prevalent in severe COVID-19. 2020 [internet publication]. [Full text](#)
265. Rhodes JM, Subramanian S, Laird E, et al. Editorial: low population mortality from COVID-19 in countries south of latitude 35 degrees North supports vitamin D as a factor determining severity. *Aliment Pharmacol Ther.* 2020 Jun;51(12):1434-7. [Full text](#) [Abstract](#)
266. Panarese A, Shahini E. Letter: Covid-19, and vitamin D. *Aliment Pharmacol Ther.* 2020 May;51(10):993-5. [Full text](#) [Abstract](#)
267. Garg M, Al-Ani A, Mitchell H, et al. Editorial: low population mortality from COVID-19 in countries south of latitude 35 degrees North – supports vitamin D as a factor determining severity. Authors' reply. *Aliment Pharmacol Ther.* 2020 Jun;51(12):1438-9. [Full text](#) [Abstract](#)
268. Marik PE, Kory P, Varon J. Does vitamin D status impact mortality from SARS-CoV-2 infection? *Med Drug Discov.* 2020 Apr 29:100041. [Full text](#) [Abstract](#)
269. Goldstein MR, Poland GA, Graeber CW. Are certain drugs associated with enhanced mortality in COVID-19? *QJM.* 2020 Jul 1;113(7):509-10. [Full text](#) [Abstract](#)
270. Mackey K, King VJ, Gurley S, et al. Risks and impact of angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers on SARS-CoV-2 infection in adults: a living systematic review. *Ann Intern Med.* 2020 Aug 4;173(3):195-203. [Full text](#) [Abstract](#)
271. Mackey K, Kansagara D, Vela K. Update alert 4: risks and impact of angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers on SARS-CoV-2 infection in adults. *Ann Intern Med.* 2020 Sep 22 [Epub ahead of print]. [Full text](#) [Abstract](#)
272. Chan CK, Huang YS, Liao HW, et al. Renin-angiotensin-aldosterone system inhibitors and risks of SARS-CoV-2 infection: a systematic review and meta-analysis. *Hypertension.* 2020 Sep 1 [Epub ahead of print]. [Full text](#) [Abstract](#)
273. Hippisley-Cox J, Young D, Coupland C, et al. Risk of severe COVID-19 disease with ACE inhibitors and angiotensin receptor blockers: cohort study including 8.3 million people. *Heart.* 2020 Jul 31 [Epub ahead of print]. [Full text](#) [Abstract](#)
274. National Institute for Health and Care Excellence. COVID-19 rapid evidence summary: angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) in people with or at risk of COVID-19. 2020 [internet publication]. [Full text](#)
275. American Heart Association; Heart Failure Society of America; American College of Cardiology. Patients taking ACE-i and ARBs who contract COVID-19 should continue treatment, unless otherwise advised by their physician. 2020 [internet publication]. [Full text](#)
276. European Society of Cardiology Council on Hypertension. Position statement of the ESC Council on Hypertension on ACE-inhibitors and angiotensin receptor blockers. 2020 [internet publication]. [Full text](#)

277. British Cardiovascular Society; British Society for Heart Failure. BSH & BCS joint statement on ACEi or ARB in relation to COVID-19. 2020 [internet publication]. [Full text](#)
278. Kow CS, Hasan SS. Meta-analysis of effect of statins in patients with COVID-19. *Am J Cardiol*. 2020 Aug 12 [Epub ahead of print]. [Full text](#) [Abstract](#)
279. Zhang XJ, Qin JJ, Cheng X, et al. In-hospital use of statins is associated with a reduced risk of mortality among individuals with COVID-19. *Cell Metab*. 2020 Aug 4;32(2):176-87. [Full text](#) [Abstract](#)
280. Almario CV, Chey WD, Spiegel BMR. Increased risk of COVID-19 among users of proton pump inhibitors. *Am J Gastroenterol*. 2020 Aug 25 [Epub ahead of print]. [Abstract](#)
281. Lee SW, Ha EK, Yeniova AÖ, et al. Severe clinical outcomes of COVID-19 associated with proton pump inhibitors: a nationwide cohort study with propensity score matching. *Gut*. 2020 Jul 30 [Epub ahead of print]. [Full text](#) [Abstract](#)
282. Costenaro P, Minotti C, Barbieri E, et al. SARS-CoV-2 infection in people living with HIV: a systematic review. *Rev Med Virol*. 2020 Sep 1:e2155. [Full text](#) [Abstract](#)
283. Emmi G, Bettiol A, Mattioli I, et al. SARS-CoV-2 infection among patients with systemic autoimmune diseases. *Autoimmun Rev*. 2020 Jul;19(7):102575. [Full text](#) [Abstract](#)
284. Favalli EG, Gerosa M, Murgo A, et al. Are patients with systemic lupus erythematosus at increased risk for COVID-19? *Ann Rheum Dis*. 2020 May 25 [Epub ahead of print]. [Full text](#) [Abstract](#)
285. Zhong J, Shen G, Yang H, et al. COVID-19 in patients with rheumatic disease in Hubei province, China: a multicentre retrospective observational study. *Lancet Rheumatol*. 2020 Jul 3 [Epub ahead of print]. [Full text](#) [Abstract](#)
286. 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. *J Infect*. 2020 Sep;81(3):e93-5. [Full text](#) [Abstract](#)
287. Fredi M, Cavazzana I, Moschetti L, et al. COVID-19 in patients with rheumatic diseases in northern Italy: a single-centre observational and case-control study. *Lancet Rheumatol*. 2020 Sep;2(9):e549-56. [Full text](#) [Abstract](#)
288. Louapre C, Collongues N, Stankoff B, et al. Clinical characteristics and outcomes in patients with coronavirus disease 2019 and multiple sclerosis. *JAMA Neurol*. 2020 Jun 26 [Epub ahead of print]. [Full text](#) [Abstract](#)
289. Aziz M, Fatima R, Haghbin H, et al. The incidence and outcomes of COVID-19 in IBD patients: a rapid review and meta-analysis. *Inflamm Bowel Dis*. 2020 Jul 3 [Epub ahead of print]. [Full text](#) [Abstract](#)
290. Golinelli D, Boetto E, Maietti E, et al. The association between ABO blood group and SARS-CoV-2 infection: a meta-analysis. *PLoS One*. 2020 Sep 18;15(9):e0239508. [Full text](#) [Abstract](#)
291. Ellinghaus D, Degenhardt F, Bujanda L, et al. Genomewide association study of severe Covid-19 with respiratory failure. *N Engl J Med*. 2020 Jun 17 [Epub ahead of print]. [Full text](#) [Abstract](#)

292. Dhar D, Mohanty A. Gut microbiota and Covid-19- possible link and implications. *Virus Res.* 2020 May 13;285:198018. [Full text](#) [Abstract](#)
293. Zuo T, Zhang F, Lui GCY, et al. Alterations in gut microbiota of patients with COVID-19 during time of hospitalization. *Gastroenterology.* 2020 May 19 [Epub ahead of print]. [Full text](#) [Abstract](#)
294. Gu S, Chen Y, Wu Z, et al. Alterations of the gut microbiota in patients with COVID-19 or H1N1 influenza. *Clin Infect Dis.* 2020 Jun 4 [Epub ahead of print]. [Abstract](#)
295. World Health Organization. Infection prevention and control during health care when coronavirus disease (COVID-19) is suspected or confirmed: interim guidance. 2020 [internet publication]. [Full text](#)
296. Liu M, Cheng SZ, Xu KW, et al. Use of personal protective equipment against coronavirus disease 2019 by healthcare professionals in Wuhan, China: cross sectional study. *BMJ.* 2020 Jun 10;369:m2195. [Full text](#) [Abstract](#)
297. Centre for Evidence-Based Medicine; Greenhalgh T, Chan XH, Khunti K, et al. What is the efficacy of standard face masks compared to respirator masks in preventing COVID-type respiratory illnesses in primary care staff? 2020 [internet publication]. [Full text](#)
298. Razai MS, Doerholt K, Ladhani S, et al. Coronavirus disease 2019 (covid-19): a guide for UK GPs. *BMJ.* 2020 Mar 5;368:m800. [Full text](#) [Abstract](#)
299. World Health Organization. Coronavirus disease (COVID-19) advice for the public. 2020 [internet publication]. [Full text](#)
300. Centers for Disease Control and Prevention. How to protect yourself and others. 2020 [internet publication]. [Full text](#)
301. Centre for Evidence-Based Medicine; Heneghan C, Jefferson T. COVID-19 evidence is lacking for 2 meter distancing. 2020 [internet publication]. [Full text](#)
302. Feng S, Shen C, Xia N, et al. Rational use of face masks in the COVID-19 pandemic. *Lancet Respir Med.* 2020 May;8(5):434-6. [Full text](#) [Abstract](#)
303. Mahase E. Covid-19: what is the evidence for cloth masks? *BMJ.* 2020 Apr 7;369:m1422. [Full text](#) [Abstract](#)
304. Chou R, Dana T, Jungbauer R, et al. Masks for prevention of respiratory virus infections, including SARS-CoV-2, in health care and community settings: a living rapid review. *Ann Intern Med.* 2020 Jul 20 [Epub ahead of print]. [Full text](#) [Abstract](#)
305. World Health Organization. Advice on the use of masks for children in the community in the context of COVID-19. 2020 [internet publication]. [Full text](#)
306. Centers for Disease Control and Prevention. Recommendation regarding the use of cloth face coverings, especially in areas of significant community-based transmission. 2020 [internet publication]. [Full text](#)

307. Lazzarino AI, Steptoe A, Hamer M, et al. Covid-19: important potential side effects of wearing face masks that we should bear in mind. *BMJ*. 2020 May 21;369:m2003. [Full text](#) [Abstract](#)
308. MacIntyre CR, Seale H, Dung TC, et al. A cluster randomised trial of cloth masks compared with medical masks in healthcare workers. *BMJ Open*. 2015 Apr 22;5(4):e006577. [Full text](#) [Abstract](#)
309. Chughtai AA, Seale H, Macintyre CR. Effectiveness of cloth masks for protection against severe acute respiratory syndrome coronavirus 2. *Emerg Infect Dis*. 2020 Jul 8;26(10). [Full text](#) [Abstract](#)
310. Centers for Disease Control and Prevention. Serious adverse health events associated with methanol-based hand sanitizers. 2020 [internet publication]. [Full text](#)
311. Mahmood A, Eqan M, Pervez S, et al. COVID-19 and frequent use of hand sanitizers; human health and environmental hazards by exposure pathways. *Sci Total Environ*. 2020 Jun 27;742:140561. [Full text](#) [Abstract](#)
312. Quilty BJ, Clifford S, CMMID nCoV working group2, et al. Effectiveness of airport screening at detecting travellers infected with novel coronavirus (2019-nCoV). *Eurosurveillance*. 2020 Feb;25(5). [Full text](#)
313. Hoehl S, Berger A, Kortenbusch M, et al. Evidence of SARS-CoV-2 infection in returning travelers from Wuhan, China. *N Engl J Med*. 2020 Mar 26;382(13):1278-80. [Full text](#) [Abstract](#)
314. Kakimoto K, Kamiya H, Yamagishi T, et al. Initial investigation of transmission of COVID-19 among crew members during quarantine of a cruise ship: Yokohama, Japan, February 2020. *MMWR Morb Mortal Wkly Rep*. 2020 Mar 20;69(11):312-3. [Full text](#) [Abstract](#)
315. Mahase E. China coronavirus: what do we know so far? *BMJ*. 2020 Jan 24;368:m308. [Full text](#) [Abstract](#)
316. Brooks SK, Webster RK, Smith LE, et al. The psychological impact of quarantine and how to reduce it: rapid review of the evidence. *Lancet*. 2020 Mar 14;395(10227):912-20. [Full text](#) [Abstract](#)
317. Nussbaumer-Streit B, Mayr V, Dobrescu AI, et al. Quarantine alone or in combination with other public health measures to control COVID-19: a rapid review. *Cochrane Database Syst Rev*. 2020 Apr 8; (4):CD013574. [Full text](#) [Abstract](#)
318. Centre for Evidence-Based Medicine; Mahtani KR, Heneghan C, Aronson JK. What is the evidence for social distancing during global pandemics? 2020 [internet publication]. [Full text](#)
319. Lewnard JA, Lo NC. Scientific and ethical basis for social-distancing interventions against COVID-19. *Lancet Infect Dis*. 2020 Jun;20(6):631-3. [Full text](#) [Abstract](#)
320. Koo JR, Cook AR, Park M, et al. Interventions to mitigate early spread of SARS-CoV-2 in Singapore: a modelling study. *Lancet Infect Dis*. 2020 Jun;20(6):678-88. [Full text](#) [Abstract](#)
321. Public Health England. Guidance on shielding and protecting people who are clinically extremely vulnerable from COVID-19. 2020 [internet publication]. [Full text](#)

322. Mahase E. Covid-19: what do we know so far about a vaccine? *BMJ*. 2020 Apr 27;369:m1679. [Full text](#)
323. Burki TK. The Russian vaccine for COVID-19. *Lancet Respir Med*. 2020 Sep 4 [Epub ahead of print]. [Full text](#) [Abstract](#)
324. Logunov DY, Dolzhikova IV, Zubkova OV, et al. Safety and immunogenicity of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine in two formulations: two open, non-randomised phase 1/2 studies from Russia. *Lancet*. 2020 Sep 3 [Epub ahead of print]. [Full text](#) [Abstract](#)
325. Padron-Regalado E. Vaccines for SARS-CoV-2: lessons from other coronavirus strains. *Infect Dis Ther*. 2020 Apr 23;:1-20. [Full text](#) [Abstract](#)
326. Hotez PJ, Corry DB, Bottazzi ME. COVID-19 vaccine design: the Janus face of immune enhancement. *Nat Rev Immunol*. 2020 Jun;20(6):347-8. [Full text](#) [Abstract](#)
327. Callaway E. Coronavirus vaccine trials have delivered their first results - but their promise is still unclear. *Nature*. 2020 May;581(7809):363-4. [Full text](#) [Abstract](#)
328. Zhu FC, Li YH, Guan XH, et al. Safety, tolerability, and immunogenicity of a recombinant adenovirus type-5 vectored COVID-19 vaccine: a dose-escalation, open-label, non-randomised, first-in-human trial. *Lancet*. 2020 Jun 13;395(10240):1845-54. [Full text](#) [Abstract](#)
329. Zhu FC, Guan XH, Li YH, et al. Immunogenicity and safety of a recombinant adenovirus type-5-vectored COVID-19 vaccine in healthy adults aged 18 years or older: a randomised, double-blind, placebo-controlled, phase 2 trial. *Lancet*. 2020 Jul 20 [Epub ahead of print]. [Full text](#) [Abstract](#)
330. van Doremalen N, Lambe T, Spencer A, et al. ChAdOx1 nCoV-19 vaccination prevents SARS-CoV-2 pneumonia in rhesus macaques. *bioRxiv*. 2020 May 13 [Epub ahead of print]. [Full text](#) [Abstract](#)
331. Folegatti PM, Ewer KJ, Aley PK, et al. Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomised controlled trial. *Lancet*. 2020 Jul 20;: . [Full text](#) [Abstract](#)
332. AstraZeneca. Statement on AstraZeneca Oxford SARS-CoV-2 vaccine, AZD1222, COVID-19 vaccine trials temporary pause. 2020 [internet publication]. [Full text](#)
333. AstraZeneca. COVID-19 vaccine AZD1222 clinical trials resumed in the UK. 2020 [internet publication]. [Full text](#)
334. Gao Q, Bao L, Mao H, et al. Development of an inactivated vaccine candidate for SARS-CoV-2. *Science*. 2020 Jul 3;369(6499):77-81. [Full text](#) [Abstract](#)
335. Xia S, Duan K, Zhang Y, et al. Effect of an inactivated vaccine against SARS-CoV-2 on safety and immunogenicity outcomes: interim analysis of 2 randomized clinical trials. *JAMA*. 2020 Aug 13 [Epub ahead of print]. [Full text](#) [Abstract](#)

336. Jackson LA, Anderson EJ, Roupael NG, et al. An mRNA vaccine against SARS-CoV-2: preliminary report. *N Engl J Med*. 2020 Jul 14 [Epub ahead of print]. [Full text](#) [Abstract](#)
337. Keech C, Albert G, Cho I, et al. Phase 1–2 trial of a SARS-CoV-2 recombinant spike protein nanoparticle vaccine. 2020 Sep 2 [Epub ahead of print]. [Full text](#) [Abstract](#)
338. Mulligan MJ, Lyke KE, Kitchin N, et al; medRxiv. The incidence and outcomes of COVID-19 in IBD patients: a rapid review and meta-analysis phase 1/2 study to describe the safety and immunogenicity of a COVID-19 RNA vaccine candidate (BNT162b1) in adults 18 to 55 years of age: interim report. 2020 [internet publication]. [Full text](#)
339. US Food and Drug Administration. Development and licensure of vaccines to prevent COVID-19. 2020 [internet publication]. [Full text](#)
340. World Health Organization. "Immunity passports" in the context of COVID-19: scientific brief. 2020 [internet publication]. [Full text](#)
341. Kofler N, Baylis F. Ten reasons why immunity passports are a bad idea. *Nature*. 2020 May;581(7809):379-81. [Full text](#) [Abstract](#)
342. Patanavanich R, Glantz SA. Smoking is associated with COVID-19 progression: a meta-analysis. *Nicotine Tob Res*. 2020 May 13 [Epub ahead of print]. [Full text](#) [Abstract](#)
343. Department of Health and Social Care. Everyone in the United Kingdom with symptoms now eligible for coronavirus tests. 2020 [internet publication]. [Full text](#)
344. Struyf T, Deeks JJ, Dinnes J, et al. Signs and symptoms to determine if a patient presenting in primary care or hospital outpatient settings has COVID-19 disease. *Cochrane Database Syst Rev*. 2020 Jul 7; (7):CD013665. [Full text](#) [Abstract](#)
345. World Health Organization. Diagnostic testing for SARS-CoV-2: interim guidance. 2020 [internet publication]. [Full text](#)
346. Liguoro I, Pilotto C, Bonanni M, et al. SARS-COV-2 infection in children and newborns: a systematic review. *Eur J Pediatr*. 2020 Jul;179(7):1029-46. [Full text](#) [Abstract](#)
347. World Health Organization. Multisystem inflammatory syndrome in children and adolescents temporally related to COVID-19: scientific brief. 2020 [internet publication]. [Full text](#)
348. British Society of Thoracic Imaging. Thoracic imaging in COVID-19 infection: guidance for the reporting radiologist - version 2. 2020 [internet publication]. [Full text](#)
349. Yang BY, Barnard LM, Emert JM, et al. Clinical characteristics of patients with coronavirus disease 2019 (COVID-19) receiving emergency medical services in King County, Washington. *JAMA Netw Open*. 2020 Jul 1;3(7):e2014549. [Full text](#) [Abstract](#)
350. Sommer P, Lukovic E, Fagley E, et al. Initial clinical impressions of the critical care of COVID-19 patients in Seattle, New York City, and Chicago. *Anesth Analg*. 2020 Jul;131(1):55-60. [Full text](#) [Abstract](#)

351. Goyal P, Choi JJ, Pinheiro LC, et al. Clinical characteristics of Covid-19 in New York City. *N Engl J Med*. 2020 Jun 11;382(24):2372-4. [Full text](#) [Abstract](#)
352. Lechien JR, Chiesa-Estomba CM, Place S, et al. Clinical and epidemiological characteristics of 1,420 European patients with mild-to-moderate coronavirus disease 2019. *J Intern Med*. 2020 Apr 30 [Epub ahead of print]. [Full text](#) [Abstract](#)
353. Matar R, Alrahmani L, Monzer N, et al. Clinical presentation and outcomes of pregnant women with COVID-19: a systematic review and meta-analysis. *Clin Infect Dis*. 2020 Jun 23 [Epub ahead of print]. [Full text](#) [Abstract](#)
354. Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ*. 2020 Sep 1;370:m3320. [Full text](#) [Abstract](#)
355. Lechien JR, Chetrit A, Chekkoury-Idrissi Y, et al. Parotitis-like symptoms associated with COVID-19, France, March-April 2020. *Emerg Infect Dis*. 2020 Jun 3;26(9). [Full text](#) [Abstract](#)
356. Martín Carreras-Presas C, Amaro Sánchez J, López-Sánchez AF, et al. Oral vesiculobullous lesions associated with SARS-CoV-2 infection. *Oral Dis*. 2020 May 5 [Epub ahead of print]. [Full text](#) [Abstract](#)
357. Marinho PM, Marcos AAA, Romano AC, et al. Retinal findings in patients with COVID-19. *Lancet*. 2020 May 23;395(10237):1610. [Full text](#) [Abstract](#)
358. Wambier CG, Vaño-Galván S, McCoy J, et al. Androgenetic alopecia present in the majority of hospitalized COVID-19 patients: the "Gabrin sign". *J Am Acad Dermatol*. 2020 May 21;83(2):680-2. [Full text](#) [Abstract](#)
359. Davis B, Rothrock AN, Swetland S, et al. Viral and atypical respiratory co-infections in COVID-19: a systematic review and meta-analysis. *J Am Coll Emerg Physicians Open*. 2020 Jun 19 [Epub ahead of print]. [Full text](#) [Abstract](#)
360. Lansbury L, Lim B, Baskaran V, et al. Co-infections in people with COVID-19: a systematic review and meta-analysis. *J Infect*. 2020 May 27 [Epub ahead of print]. [Full text](#) [Abstract](#)
361. Langford BJ, So M, Raybardhan S, et al. Bacterial co-infection and secondary infection in patients with COVID-19: a living rapid review and meta-analysis. *Clin Microbiol Infect*. 2020 Jul 22 [Epub ahead of print]. [Full text](#) [Abstract](#)
362. Gayam V, Konala VM, Naramala S, et al. Presenting characteristics, comorbidities, and outcomes of patients coinfecting with COVID-19 and *Mycoplasma pneumoniae* in the USA. *J Med Virol*. 2020 May 25 [Epub ahead of print]. [Full text](#) [Abstract](#)
363. Ding Q, Lu P, Fan Y, et al. The clinical characteristics of pneumonia patients co-infected with 2019 novel coronavirus and influenza virus in Wuhan, China. *J Med Virol*. 2020 Mar 20 [Epub ahead of print]. [Full text](#) [Abstract](#)
364. Cuadrado-Payán E, Montagud-Marrahi E, Torres-Elorza M, et al. SARS-CoV-2 and influenza virus co-infection. *Lancet*. 2020 May 16;395(10236):e84. [Full text](#) [Abstract](#)

365. Cui X, Zhao Z, Zhang T, et al. A systematic review and meta-analysis of children with coronavirus disease 2019 (COVID-19). *J Med Virol*. 2020 Aug 6 [Epub ahead of print]. [Full text](#) [Abstract](#)
366. Li Y, Wang H, Wang F, et al. Comparison of hospitalized patients with pneumonia caused by COVID-19 and influenza A in children under 5 years. *Int J Infect Dis*. 2020 Jun 11;98:80-3. [Full text](#) [Abstract](#)
367. Cook J, Harman K, Zoica B, et al. Horizontal transmission of severe acute respiratory syndrome coronavirus 2 to a premature infant: multiple organ injury and association with markers of inflammation. *Lancet Child Adolesc Health*. 2020 Jul;4(7):548-51. [Full text](#) [Abstract](#)
368. Shekerdemian LS, Mahmood NR, Wolfe KK, et al. Characteristics and outcomes of children with coronavirus disease 2019 (COVID-19) infection admitted to US and Canadian pediatric intensive care units. *JAMA Pediatr*. 2020 May 11 [Epub ahead of print]. [Full text](#) [Abstract](#)
369. Williams N, Radia T, Harman K, et al. COVID-19 severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children and adolescents: a systematic review of critically unwell children and the association with underlying comorbidities. *Eur J Pediatr*. 2020 Sep 10 [Epub ahead of print]. [Full text](#) [Abstract](#)
370. Lorenz N, Treptow A, Schmidt S, et al. Neonatal early-onset infection with SARS-CoV-2 in a newborn presenting with encephalitic symptoms. *Pediatr Infect Dis J*. 2020 Aug;39(8):e212. [Abstract](#)
371. Chacón-Aguilar R, Osorio-Cámara JM, Sanjurjo-Jimenez I, et al. COVID-19: fever syndrome and neurological symptoms in a neonate. *An Pediatr (Engl Ed)*. 2020 Apr 27;92(6):373-4. [Full text](#) [Abstract](#)
372. Sinelli MT, Paterlini G, Citterio M, et al. Early neonatal SARS-CoV-2 infection manifesting with hypoxemia requiring respiratory support. *Pediatrics*. 2020 Jul;146(1):e20201121. [Full text](#) [Abstract](#)
373. Xia W, Shao J, Guo Y, et al. Clinical and CT features in pediatric patients with COVID-19 infection: different points from adults. *Pediatr Pulmonol*. 2020 May;55(5):1169-74. [Full text](#) [Abstract](#)
374. Ikeuchi K, Saito M, Yamamoto S, et al. Relative bradycardia in patients with mild-to-moderate coronavirus disease, Japan. *Emerg Infect Dis*. 2020 Jul 1;26(10). [Full text](#) [Abstract](#)
375. Xie J, Tong Z, Guan X, et al. Critical care crisis and some recommendations during the COVID-19 epidemic in China. *Intensive Care Med*. 2020 May;46(5):837-40. [Full text](#) [Abstract](#)
376. Royal College of Physicians. NEWS2 and deterioration in COVID-19. 2020 [internet publication]. [Full text](#)
377. Li LQ, Huang T, Wang YQ, et al. COVID-19 patients' clinical characteristics, discharge rate, and fatality rate of meta-analysis. *J Med Virol*. 2020 Jun;92(6):577-83. [Full text](#) [Abstract](#)
378. Zhu J, Zhong Z, Ji P, et al. Clinicopathological characteristics of 8697 patients with COVID-19 in China: a meta-analysis. *Fam Med Community Health*. 2020 Apr;8(2). [Full text](#) [Abstract](#)

379. Zhang ZL, Hou YL, Li DT, et al. Laboratory findings of COVID-19: a systematic review and meta-analysis. *Scand J Clin Lab Invest*. 2020 May 23;1-7. [Full text](#) [Abstract](#)
380. Wu H, Zhu H, Yuan C, et al. Clinical and immune features of hospitalized pediatric patients with coronavirus disease 2019 (COVID-19) in Wuhan, China. *JAMA Netw Open*. 2020 Jun 1;3(6):e2010895. [Full text](#) [Abstract](#)
381. Henry BM, Benoit SW, de Oliveira MHS, et al. Laboratory abnormalities in children with mild and severe coronavirus disease 2019 (COVID-19): a pooled analysis and review. *Clin Biochem*. 2020 Jul;81:1-8. [Full text](#) [Abstract](#)
382. Kronbichler A, Kresse D, Yoon S, et al. Asymptomatic patients as a source of COVID-19 infections: a systematic review and meta-analysis. *Int J Infect Dis*. 2020 Jun 17 [Epub ahead of print]. [Full text](#) [Abstract](#)
383. Public Health England. COVID-19: investigation and initial clinical management of possible cases. 2020 [internet publication]. [Full text](#)
384. Centers for Disease Control and Prevention. Overview of testing for SARS-CoV-2 (COVID-19). 2020 [internet publication]. [Full text](#)
385. Azzi L, Carcano G, Gianfagna F, et al. Saliva is a reliable tool to detect SARS-CoV-2. *J Infect*. 2020 Apr 13 [Epub ahead of print]. [Full text](#) [Abstract](#)
386. Williams E, Bond K, Zhang B, et al. Saliva as a non-invasive specimen for detection of SARS-CoV-2. *J Clin Microbiol*. 2020 Apr 21 [Epub ahead of print]. [Full text](#) [Abstract](#)
387. Caulley L, Corsten M, Eapen L, et al. Salivary detection of COVID-19. *Ann Intern Med*. 2020 Aug 28 [Epub ahead of print]. [Full text](#) [Abstract](#)
388. Wyllie AL, Fournier J, Casanovas-Massana A, et al. Saliva or nasopharyngeal swab specimens for detection of SARS-CoV-2. *N Engl J Med*. 2020 Aug 28 [Epub ahead of print]. [Full text](#) [Abstract](#)
389. Centers for Disease Control and Prevention. Interim guidelines for collecting, handling, and testing clinical specimens for COVID-19. 2020 [internet publication]. [Full text](#)
390. Wu X, Cai Y, Huang X, et al. Co-infection with SARS-CoV-2 and influenza A virus in patient with pneumonia, China. *Emerg Infect Dis*. 2020 Mar 11;26(6). [Full text](#) [Abstract](#)
391. Centre for Evidence-Based Medicine; Jefferson T, Heneghan C, Spencer EA, et al. Are you infectious if you have a positive PCR test result for COVID-19? 2020 [internet publication]. [Full text](#)
392. Jefferson T, Spencer E, Brassey J, et al; medRxiv. Viral cultures for COVID-19 infectivity assessment: systematic review. 2020 [internet publication]. [Full text](#)
393. Floriano I, Silvinato A, Bernardo WM, et al. Accuracy of the polymerase chain reaction (PCR) test in the diagnosis of acute respiratory syndrome due to coronavirus: a systematic review and meta-analysis. *Rev Assoc Med Bras (1992)*. 2020 Jul;66(7):880-8. [Full text](#) [Abstract](#)

394. Watson J, Whiting PF, Brush JE. Interpreting a covid-19 test result. *BMJ*. 2020 May 12;369:m1808. [Full text](#) [Abstract](#)
395. Public Health Laboratory Network. PHLN statement on nucleic acid test false positive results for SARS-CoV-2. 2020 [internet publication]. [Full text](#)
396. US Food and Drug Administration. CDC 2019-novel coronavirus (2019-nCoV) real-time RT-PCR diagnostic panel. 2020 [internet publication]. [Full text](#)
397. Australian Government Department of Health. COVID-19 testing in Australia: information for health professionals. 2020 [internet publication]. [Full text](#)
398. Kucirka LM, Lauer SA, Laeyendecker O, et al. Variation in false-negative rate of reverse transcriptase polymerase chain reaction–based SARS-CoV-2 tests by time since exposure. *Ann Intern Med*. 2020 May 13 [Epub ahead of print]. [Full text](#) [Abstract](#)
399. Watson J, Richter A, Deeks J. Testing for SARS-CoV-2 antibodies. *BMJ*. 2020 Sep 8;370:m3325. [Full text](#) [Abstract](#)
400. Centers for Disease Control and Prevention. Interim guidelines for COVID-19 antibody testing. 2020 [internet publication]. [Full text](#)
401. Infectious Diseases Society of America. Infectious Diseases Society of America guidelines on the diagnosis of COVID-19: serologic testing. 2020 [internet publication]. [Full text](#)
402. Long QX, Liu BZ, Deng HJ, et al. Antibody responses to SARS-CoV-2 in patients with COVID-19. *Nat Med*. 2020 Jun;26(6):845-8. [Full text](#) [Abstract](#)
403. Qu J, Wu C, Li X, et al. Profile of IgG and IgM antibodies against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). *Clin Infect Dis*. 2020 Apr 27 [Epub ahead of print]. [Full text](#) [Abstract](#)
404. Deeks JJ, Dinnes J, Takwoingi Y, et al. Antibody tests for identification of current and past infection with SARS-CoV-2. *Cochrane Database Syst Rev*. 2020 Jun 25;(6):CD013652. [Full text](#) [Abstract](#)
405. World Health Organization. Advice on the use of point-of-care immunodiagnostic tests for COVID-19: scientific brief. 2020 [internet publication]. [Full text](#)
406. Lisboa Bastos M, Tavaziva G, Abidi SK, et al. Diagnostic accuracy of serological tests for covid-19: systematic review and meta-analysis. *BMJ*. 2020 Jul 1;370:m2516. [Full text](#) [Abstract](#)
407. World Health Organization. Antigen-detection in the diagnosis of SARS-CoV-2 infection using rapid immunoassays: interim guidance. 2020 [internet publication]. [Full text](#)
408. Poon LC, Yang H, Kapur A, et al. Global interim guidance on coronavirus disease 2019 (COVID-19) during pregnancy and puerperium from FIGO and allied partners: information for healthcare professionals. 2020 [internet publication]. [Full text](#)
409. Song F, Shi N, Shan F, et al. Emerging coronavirus 2019-nCoV pneumonia. *Radiology*. 2020 Feb 6:200274. [Full text](#) [Abstract](#)

410. World Health Organization. Use of chest imaging in COVID-19: a rapid advice guide. 2020 [internet publication]. [Full text](#)
411. Tavare AN, Braddy A, Brill S, et al. Managing high clinical suspicion COVID-19 inpatients with negative RT-PCR: a pragmatic and limited role for thoracic CT. *Thorax*. 2020 Jul;75(7):537-8. [Full text](#) [Abstract](#)
412. American College of Radiology. ACR recommendations for the use of chest radiography and computed tomography (CT) for suspected COVID-19 infection. 2020 [internet publication]. [Full text](#)
413. Sun P, Qie S, Liu Z, et al. Clinical characteristics of hospitalized patients with SARS-CoV-2 infection: a single arm meta-analysis. *J Med Virol*. 2020 Jun;92(6):612-7. [Full text](#) [Abstract](#)
414. Li Z, Yi Y, Luo X, et al. Development and clinical application of a rapid IgM-IgG combined antibody test for SARS-CoV-2 infection diagnosis. *J Med Virol*. 2020 Feb 27 [Epub ahead of print]. [Abstract](#)
415. Tsikala Vafea M, Atalla E, Kalligeros M, et al. Chest CT findings in asymptomatic cases with COVID-19: a systematic review and meta-analysis. *Clin Radiol*. 2020 Aug 12 [Epub ahead of print]. [Full text](#) [Abstract](#)
416. Yang W, Cao Q, Qin L, et al. Clinical characteristics and imaging manifestations of the 2019 novel coronavirus disease (COVID-19): a multi-center study in Wenzhou city, Zhejiang, China. *J Infect*. 2020 Apr;80(4):388-93. [Full text](#) [Abstract](#)
417. Long C, Xu H, Shen Q, et al. Diagnosis of the coronavirus disease (COVID-19): rRT-PCR or CT? *Eur J Radiol*. 2020 Mar 25;126:108961. [Full text](#) [Abstract](#)
418. Ojha V, Mani A, Pandey NN, et al. CT in coronavirus disease 2019 (COVID-19): a systematic review of chest CT findings in 4410 adult patients. *Eur Radiol*. 2020 May 30 [Epub ahead of print]. [Full text](#) [Abstract](#)
419. Zhao D, Yao F, Wang L, et al. A comparative study on the clinical features of COVID-19 pneumonia to other pneumonias. *Clin Infect Dis*. 2020 Mar 12 [Epub ahead of print]. [Full text](#) [Abstract](#)
420. Kumar J, Meena J, Yadav A, et al. Radiological findings of COVID-19 in children: a systematic review and meta-analysis. *J Trop Pediatr*. 2020 Jul 21 [Epub ahead of print]. [Full text](#) [Abstract](#)
421. Park GS, Ku K, Baek SH, et al. Development of reverse transcription loop-mediated isothermal amplification assays targeting severe acute respiratory syndrome coronavirus 2. *J Mol Diagn*. 2020 Jun;22(6):729-35. [Full text](#) [Abstract](#)
422. Baek YH, Um J, Antigua KJC, et al. Development of a reverse transcription-loop-mediated isothermal amplification as a rapid early-detection method for novel SARS-CoV-2. *Emerg Microbes Infect*. 2020 Apr 20:1-31. [Full text](#) [Abstract](#)
423. Lu R, Wu X, Wan Z, et al. A novel reverse transcription loop-mediated isothermal amplification method for rapid detection of SARS-CoV-2. *Int J Mol Sci*. 2020 Apr 18;21(8). [Full text](#) [Abstract](#)

424. Mohamed MFH, Al-Shokri S, Yousaf Z, et al. Frequency of abnormalities detected by point-of-care lung ultrasound in symptomatic COVID-19 patients: systematic review and meta-analysis. *Am J Trop Med Hyg.* 2020 Jun 2 [Epub ahead of print]. [Full text](#) [Abstract](#)
425. Moro F, Buonsenso D, Moruzzi MC, et al. How to perform lung ultrasound in pregnant women with suspected COVID-19 infection. *Ultrasound Obstet Gynecol.* 2020 May;55(5):593-8. [Full text](#) [Abstract](#)
426. Denina M, Scolfaro C, Silvestro E, et al. Lung ultrasound in children with COVID-19. *Pediatrics.* 2020 Jul;146(1):e20201157. [Full text](#) [Abstract](#)
427. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med.* 2020 Apr 30;382(18):1708-20. [Full text](#) [Abstract](#)
428. Lu X, Zhang L, Du H, et al. SARS-CoV-2 infection in children. *N Engl J Med.* 2020 Apr 23;382(17):1663-5. [Full text](#) [Abstract](#)
429. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA.* 2020 Feb 7;323(11):1061-9. [Full text](#) [Abstract](#)
430. Grant MC, Geoghegan L, Arbyn M, et al. The prevalence of symptoms in 24,410 adults infected by the novel coronavirus (SARS-CoV-2; COVID-19): a systematic review and meta-analysis of 148 studies from 9 countries. *PLoS One.* 2020 Jun 23;15(6):e0234765. [Full text](#) [Abstract](#)
431. Agyeman AA, Chin KL, Landersdorfer CB, et al. Smell and taste dysfunction in patients with COVID-19: a systematic review and meta-analysis. *Mayo Clin Proc.* 2020 Aug;95(8):1621-31. [Full text](#) [Abstract](#)
432. Eliezer M, Hautefort C, Hamel AL, et al. Sudden and complete olfactory loss function as a possible symptom of COVID-19. *JAMA Otolaryngol Head Neck Surg.* 2020 Apr 8 [Epub ahead of print]. [Full text](#) [Abstract](#)
433. Boscolo-Rizzo P, Borsetto D, Fabbris C, et al. Evolution of altered sense of smell or taste in patients with mildly symptomatic COVID-19. *JAMA Otolaryngol Head Neck Surg.* 2020 Jul 2 [Epub ahead of print]. [Abstract](#)
434. Tariq R, Saha S, Furqan F, et al. Prevalence and mortality of COVID-19 patients with gastrointestinal symptoms: a systematic review and meta-analysis. *Mayo Clin Proc.* 2020 Aug;95(8):1632-48. [Full text](#) [Abstract](#)
435. Chen A, Agarwal A, Ravindran N, et al. Are gastrointestinal symptoms specific for COVID-19 infection? A prospective case-control study from the United States. *Gastroenterology.* 2020 May 15 [Epub ahead of print]. [Full text](#) [Abstract](#)
436. Guotao L, Xingpeng Z, Zhihui D, et al. SARS-CoV-2 infection presenting with hematochezia. *Med Mal Infect.* 2020 May;50(3):293-6. [Full text](#) [Abstract](#)
437. Helms J, Kremer S, Merdji H, et al. Neurologic features in severe SARS-CoV-2 infection. *N Engl J Med.* 2020 Jun 4;382(23):2268-70. [Full text](#) [Abstract](#)

438. Chen T, Wu D, Chen H, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. *BMJ*. 2020 Mar 26;368:m1091. [Full text](#) [Abstract](#)
439. Inomata T, Kitazawa K, Kuno T, et al. Clinical and prodromal ocular symptoms in coronavirus disease: a systematic review and meta-analysis. *Invest Ophthalmol Vis Sci*. 2020 Aug 3;61(10):29. [Full text](#) [Abstract](#)
440. Ma N, Li P, Wang X, et al. Ocular manifestations and clinical characteristics of children with laboratory-confirmed COVID-19 in Wuhan, China. *JAMA Ophthalmol*. 2020 Aug 26 [Epub ahead of print]. [Full text](#) [Abstract](#)
441. Bandhala Rajan M, Kumar-M P, Bhardwaj A. The trend of cutaneous lesions during COVID-19 pandemic: lessons from a meta-analysis and systematic review. *Int J Dermatol*. 2020 Sep 16 [Epub ahead of print]. [Full text](#) [Abstract](#)
442. Bataille V, Visconti A, Rossi R, et al; medRxiv. Diagnostic value of skin manifestation of SARS-CoV-2 infection. 2020 [internet publication]. [Full text](#)
443. Casey K, Iteen A, Nicolini R, et al. COVID-19 pneumonia with hemoptysis: acute segmental pulmonary emboli associated with novel coronavirus infection. *Am J Emerg Med*. 2020 Jul;38(7):1544. [Full text](#) [Abstract](#)
444. Centers for Disease Control and Prevention. CDC's diagnostic multiplex assay for flu and COVID-19 and supplies. 2020 [internet publication]. [Full text](#)
445. Danwang C, Endomba FT, Nneck JR, et al. A meta-analysis of potential biomarkers associated with severity of coronavirus disease 2019 (COVID-19). *Biomark Res*. 2020 Aug 31;8:37. [Full text](#) [Abstract](#)
446. Foy BH, Carlson JCT, Reinertsen E, et al. Association of red blood cell distribution width with mortality risk in hospitalized adults with SARS-CoV-2 infection. *JAMA Netw Open*. 2020 Sep 1;3(9):e2022058. [Full text](#) [Abstract](#)
447. Huang W, Berube J, McNamara M, et al. Lymphocyte subset counts in COVID-19 patients: a meta-analysis. *Cytometry A*. 2020 Jun 15 [Epub ahead of print]. [Full text](#) [Abstract](#)
448. Chen W, Li Z, Yang B, et al. Delayed-phase thrombocytopenia in patients of coronavirus disease 2019 (COVID-19). *Br J Haematol*. 2020 May 26 [Epub ahead of print]. [Full text](#) [Abstract](#)
449. Chen D, Li X, Song Q, et al. Assessment of hypokalemia and clinical characteristics in patients with coronavirus disease 2019 in Wenzhou, China. *JAMA Netw Open*. 2020 Jun 1;3(6):e2011122. [Full text](#) [Abstract](#)
450. Liu J, Han P, Wu J, et al. Prevalence and predictive value of hypocalcemia in severe COVID-19 patients. *J Infect Public Health*. 2020 Jun 22 [Epub ahead of print]. [Full text](#) [Abstract](#)
451. Ceriello A. Hyperglycemia and the worse prognosis of COVID-19: why a fast blood glucose control should be mandatory. *Diabetes Res Clin Pract*. 2020 Apr 29;163:108186. [Full text](#) [Abstract](#)

452. Bode B, Garrett V, Messler J, et al. Glycemic characteristics and clinical outcomes of COVID-19 patients hospitalized in the United States. *J Diabetes Sci Technol*. 2020 May 9:1932296820924469. [Full text](#) [Abstract](#)
453. Iacobellis G, Penaherrera CA, Bermudez LE, et al. Admission hyperglycemia and radiological findings of SARS-CoV2 in patients with and without diabetes. *Diabetes Res Clin Pract*. 2020 May 1;164:108185. [Full text](#) [Abstract](#)
454. Shah S, Shah K, Patel SB, et al. Elevated D-dimer levels are associated with increased risk of mortality in COVID-19: a systematic review and meta-analysis. *Cardiol Rev*. 2020 Jul 2 [Epub ahead of print]. [Abstract](#)
455. Leonard-Lorant I, Delabranche X, Severac F, et al. Acute pulmonary embolism in COVID-19 patients on CT angiography and relationship to D-dimer levels. *Radiology*. 2020 Apr 23:201561. [Full text](#) [Abstract](#)
456. Mucha SR, Dugar S, McCrae K, et al. Coagulopathy in COVID-19. *Cleve Clin J Med*. 2020 May 14 [Epub ahead of print]. [Abstract](#)
457. Han H, Xie L, Liu R, et al. Analysis of heart injury laboratory parameters in 273 COVID-19 patients in one hospital in Wuhan, China. *J Med Virol*. 2020 Mar 31 [Epub ahead of print]. [Full text](#) [Abstract](#)
458. Aboughdir M, Kirwin T, Abdul Khader A, et al. Prognostic value of cardiovascular biomarkers in COVID-19: a review. *Viruses*. 2020 May 11;12(5). [Full text](#) [Abstract](#)
459. Soraya GV, Ulhaq ZS. Interleukin-6 levels in children developing SARS-CoV-2 infection. *Pediatr Neonatol*. 2020 May 4 [Epub ahead of print]. [Full text](#) [Abstract](#)
460. National Institute for Health and Care Excellence. COVID-19 rapid guideline: antibiotics for pneumonia in adults in hospital. 2020 [internet publication]. [Full text](#)
461. Metlay JP, Waterer GW. Treatment of community-acquired pneumonia during the coronavirus disease 2019 (COVID-19) pandemic. *Ann Intern Med*. 2020 May 7 [Epub ahead of print]. [Full text](#) [Abstract](#)
462. Mehta P, McAuley DF, Brown M, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet*. 2020 Mar 28;395(10229):1033-4. [Full text](#) [Abstract](#)
463. Fu J, Huang PP, Zhang S, et al. The value of serum amyloid A for predicting the severity and recovery of COVID-19. *Exp Ther Med*. 2020 Oct;20(4):3571-7. [Full text](#) [Abstract](#)
464. Kim H, Hong H, Yoon SH. Diagnostic performance of CT and reverse transcriptase-polymerase chain reaction for coronavirus disease 2019: a meta-analysis. *Radiology*. 2020 Apr 17:201343. [Full text](#) [Abstract](#)
465. Lv M, Wang M, Yang N, et al. Chest computed tomography for the diagnosis of patients with coronavirus disease 2019 (COVID-19): a rapid review and meta-analysis. *Ann Transl Med*. 2020 May;8(10):622. [Full text](#) [Abstract](#)

466. Ai T, Yang Z, Hou H, et al. Correlation of chest CT and RT-PCR testing in coronavirus disease 2019 (COVID-19) in China: a report of 1014 cases. *Radiology*. 2020 Feb 26;200642. [Full text](#) [Abstract](#)
467. National Institute for Health and Care Excellence. COVID-19 rapid guideline: managing suspected or confirmed pneumonia in adults in the community. 2020 [internet publication]. [Full text](#)
468. Centre for Evidence-Based Medicine; Heneghan C, Pluddemann A, Mahtani KR. Differentiating viral from bacterial pneumonia. 2020 [internet publication]. [Full text](#)
469. Hani C, Trieu NH, Saab I, et al. COVID-19 pneumonia: a review of typical CT findings and differential diagnosis. *Diagn Interv Imaging*. 2020 May;101(5):263-8. [Full text](#) [Abstract](#)
470. Solomon DA, Sherman AC, Kanjilal S. Influenza in the COVID-19 era. *JAMA*. 2020 Aug 14 [Epub ahead of print]. [Full text](#) [Abstract](#)
471. Song X, Delaney M, Shah RK, et al. Comparison of clinical features of COVID-19 vs seasonal influenza A and B in US children. *JAMA Netw Open*. 2020 Sep 1;3(9):e2020495. [Full text](#) [Abstract](#)
472. Beltrán-Corbellini Á, Chico-García JL, Martínez-Poles J, et al. Acute-onset smell and taste disorders in the context of Covid-19: a pilot multicenter PCR-based case-control study. *Eur J Neurol*. 2020 Apr 22 [Epub ahead of print]. [Full text](#) [Abstract](#)
473. Liu M, Zeng W, Wen Y, et al. COVID-19 pneumonia: CT findings of 122 patients and differentiation from influenza pneumonia. *Eur Radiol*. 2020 May 12 [Epub ahead of print]. [Full text](#) [Abstract](#)
474. Yin Z, Kang Z, Yang D, et al. A comparison of clinical and chest CT findings in patients with influenza A (H1N1) virus infection and coronavirus disease (COVID-19). *AJR Am J Roentgenol*. 2020 May 26:1-7. [Full text](#) [Abstract](#)
475. Luo Y, Yuan X, Xue Y, et al. Using the diagnostic model based on routine laboratory tests to distinguish patients infected with SARS-CoV-2 from those infected with influenza virus. *Int J Infect Dis*. 2020 May 1;95:436-40. [Full text](#) [Abstract](#)
476. Zarei F, Reza J, Sefidbakht S, et al. Aspiration pneumonia or COVID-19 infection: a diagnostic challenge. *Acad Radiol*. 2020 May 3 [Epub ahead of print]. [Full text](#) [Abstract](#)
477. National Institute for Health and Care Excellence. COVID-19 rapid guideline: delivery of systemic anticancer treatments. 2020 [internet publication]. [Full text](#)
478. World Health Organization. Home care for patients with suspected or confirmed COVID-19 and management of their contacts: interim guidance. 2020 [internet publication]. [Full text](#)
479. World Health Organization. Updated WHO recommendations for international traffic in relation to COVID-19 outbreak. February 2020 [internet publication]. [Full text](#)
480. Arima Y, Shimada T, Suzuki M, et al. Severe acute respiratory syndrome coronavirus 2 infection among returnees to Japan from Wuhan, China, 2020. *Emerg Infect Dis*. 2020 Apr 10;26(7). [Full text](#) [Abstract](#)

481. Kwon KT, Ko JH, Shin H, et al. Drive-through screening center for COVID-19: a safe and efficient screening system against massive community outbreak. *J Korean Med Sci.* 2020 Mar 23;35(11):e123. [Full text](#) [Abstract](#)
482. Medicines and Healthcare products Regulatory Agency. Don't rely on temperature screening products for detection of coronavirus (COVID-19), says MHRA. 2020 [internet publication]. [Full text](#) [Abstract](#)
483. Centers for Disease Control and Prevention. Interim infection prevention and control recommendations for healthcare personnel during the coronavirus disease 2019 (COVID-19) pandemic. 2020 [internet publication]. [Full text](#)
484. Infectious Diseases Society of America. Infectious Diseases Society of America guidelines on the diagnosis of COVID-19. 2020 [internet publication]. [Full text](#)
485. Infectious Diseases Society of America. Infectious Diseases Society of America guidelines on infection prevention in patients with suspected or known COVID-19. 2020 [internet publication]. [Full text](#)
486. Infectious Diseases Society of America. COVID-19 real-time learning network. 2020 [internet publication]. [Full text](#)
487. American Academy of Pediatrics. Clinical guidance. 2020 [internet publication]. [Full text](#)
488. World Health Organization. Country & technical guidance - coronavirus disease (COVID-19). 2020 [internet publication]. [Full text](#)
489. Scottish Intercollegiate Guidelines Network. Assessment of COVID-19 in primary care: the identification of symptoms, signs, characteristics, comorbidities and clinical signs in adults which may indicate a higher risk of progression to severe disease. 2020 [internet publication]. [Full text](#)
490. Scottish Intercollegiate Guidelines Network. COVID-19 position statement: presentations and management of COVID-19 in older people in acute care. 2020 [internet publication]. [Full text](#)
491. Public Health England. COVID-19: guidance for health professionals. 2020 [internet publication]. [Full text](#)
492. European Centre for Disease Prevention and Control. COVID-19 pandemic. 2020 [internet publication]. [Full text](#)
493. Jin YH, Cai L, Cheng ZS, et al. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). *Mil Med Res.* 2020 Feb 6;7(1):4. [Full text](#) [Abstract](#)
494. Li T. Diagnosis and clinical management of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection: an operational recommendation of Peking Union Medical College Hospital (V2.0). *Emerg Microbes Infect.* 2020 Mar;9(1):582-5. [Full text](#) [Abstract](#)
495. National Institute for Health and Care Excellence. COVID-19 rapid guideline: critical care in adults. 2020 [internet publication]. [Full text](#)

496. National Institute for Health and Care Excellence. COVID-19 rapid guideline: managing symptoms (including at the end of life) in the community. 2020 [internet publication]. [Full text](#)
497. World Health Organization. Corticosteroids for COVID-19: living guidance. 2020 [internet publication]. [Full text](#)
498. Siemieniuk RA, Bartoszko JJ, Ge L, et al. Drug treatments for covid-19: living systematic review and network meta-analysis. *BMJ*. 2020 Jul 30;370:m2980. [Full text](#) [Abstract](#)
499. Bhimraj A, Morgan RL, Hirsch Shumaker A, et al. Infectious Diseases Society of America guidelines on the treatment and management of patients with COVID-19. 2020 [internet publication]. [Full text](#)
500. Petrilli CM, Jones SA, Yang J, et al. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. *BMJ*. 2020 May 22;369:m1966. [Full text](#) [Abstract](#)
501. Kilaru AS, Lee K, Snider CK, et al. Return hospital admissions among 1419 covid-19 patients discharged from five US emergency departments. *Acad Emerg Med*. 2020 Aug 27 [Epub ahead of print]. [Full text](#) [Abstract](#)
502. Götzinger F, Santiago-García B, Noguera-Julián A, et al. COVID-19 in children and adolescents in Europe: a multinational, multicentre cohort study. *Lancet Child Adolesc Health*. 2020 Jun 25 [Epub ahead of print]. [Full text](#) [Abstract](#)
503. Abate SM, Ahmed Ali S, Mantfardo B, et al. Rate of intensive care unit admission and outcomes among patients with coronavirus: a systematic review and meta-analysis. *PLoS One*. 2020 Jul 10;15(7):e0235653. [Full text](#) [Abstract](#)
504. Bhatraju PK, Ghassemieh BJ, Nichols M, et al. Covid-19 in critically ill patients in the Seattle region: case series. *N Engl J Med*. 2020 Mar 30 [Epub ahead of print]. [Full text](#) [Abstract](#)
505. Argenziano MG, Bruce SL, Slater CL, et al. Characterization and clinical course of 1000 patients with coronavirus disease 2019 in New York: retrospective case series. *BMJ*. 2020 May 29;369:m1996. [Full text](#) [Abstract](#)
506. Centers for Disease Control and Prevention. Discontinuation of isolation for persons with COVID-19 not in healthcare settings. 2020 [internet publication]. [Full text](#)
507. Public Health England. Guidance for stepdown of infection control precautions and discharging COVID-19 patients. 2020 [internet publication]. [Full text](#)
508. European Medicines Agency. EMA gives advice on the use of non-steroidal anti-inflammatories for COVID-19. 2020 [internet publication]. [Full text](#)
509. US Food and Drug Administration. FDA advises patients on use of non-steroidal anti-inflammatory drugs (NSAIDs) for COVID-19. 2020 [internet publication]. [Full text](#)
510. Little P. Non-steroidal anti-inflammatory drugs and covid-19. *BMJ*. 2020 Mar 27;368:m1185. [Full text](#) [Abstract](#)

511. Medicines and Healthcare products Regulatory Agency; Commission on Human Medicines. Commission on Human Medicines advice on ibuprofen and coronavirus (COVID-19). 2020 [internet publication]. [Full text](#)
512. World Health Organization. The use of non-steroidal anti-inflammatory drugs (NSAIDs) in patients with COVID-19: scientific brief. 2020 [internet publication]. [Full text](#)
513. National Institute for Health and Care Excellence. COVID-19 rapid evidence summary: acute use of non-steroidal anti-inflammatory drugs (NSAIDs) for people with or at risk of COVID-19. 2020 [internet publication]. [Full text](#)
514. Abuelgasim H, Albury C, Lee J. Effectiveness of honey for symptomatic relief in upper respiratory tract infections: a systematic review and meta-analysis. *BMJ Evid Based Med*. 2020 Aug 18 [Epub ahead of print]. [Full text](#) [Abstract](#)
515. Whitcroft KL, Hummel T. Olfactory dysfunction in COVID-19: diagnosis and management. *JAMA*. 2020 May 20 [Epub ahead of print]. [Full text](#) [Abstract](#)
516. Centers for Disease Control and Prevention. Discontinuation of transmission-based precautions and disposition of patients with COVID-19 in healthcare settings (interim guidance). 2020 [internet publication]. [Full text](#)
517. Hewitt J, Carter B, Vilches-Moraga A, et al. The effect of frailty on survival in patients with COVID-19 (COPE): a multicentre, European, observational cohort study. *Lancet Public Health*. 2020 Jun 30 [Epub ahead of print]. [Full text](#) [Abstract](#)
518. Centre for Evidence-Based Medicine; Allsop M, Ziegler L, Fu Y, et al. Is oxygen an effective treatment option to alleviate the symptoms of breathlessness for patients dying with COVID-19 and what are the potential harms? 2020 [internet publication]. [Full text](#)
519. Alhazzani W, Møller MH, Arabi YM, et al. Surviving Sepsis Campaign: guidelines on the management of critically ill adults with coronavirus disease 2019 (COVID-19). *Intensive Care Med*. 2020 May;46(5):854-87. [Full text](#) [Abstract](#)
520. NHS England. Clinical guide for the optimal use of oxygen therapy during the coronavirus pandemic. 2020 [internet publication]. [Full text](#)
521. Dondorp AM, Hayat M, Aryal D, et al. Respiratory support in novel coronavirus disease (COVID-19) patients, with a focus on resource-limited settings. *Am J Trop Med Hyg*. 2020 Apr 21 [Epub ahead of print]. [Full text](#) [Abstract](#)
522. Caputo ND, Strayer RJ, Levitan R. Early self-proning in awake, non-intubated patients in the emergency department: a single ED's experience during the COVID-19 pandemic. *Acad Emerg Med*. 2020 May;27(5):375-8. [Full text](#) [Abstract](#)
523. Ng Z, Tay WC, Ho CHB. Awake prone positioning for non-intubated oxygen dependent COVID-19 pneumonia patients. *Eur Respir J*. 2020 May 26 [Epub ahead of print]. [Full text](#) [Abstract](#)

524. Golestani-Eraghi M, Mahmoodpoor A. Early application of prone position for management of Covid-19 patients. *J Clin Anesth*. 2020 May 26;66:109917. [Full text](#) [Abstract](#)
525. Thompson AE, Ranard BL, Wei Y, et al. Prone positioning in awake, nonintubated patients with COVID-19 hypoxemic respiratory failure. *JAMA Intern Med*. 2020 Jun 17 [Epub ahead of print]. [Full text](#) [Abstract](#)
526. Coppo A, Bellani G, Winterton D, et al. Feasibility and physiological effects of prone positioning in non-intubated patients with acute respiratory failure due to COVID-19 (PRON-COVID): a prospective cohort study. *Lancet Respir Med*. 2020 Jun 19 [Epub ahead of print]. [Full text](#) [Abstract](#)
527. Mojoli F, Mongodi S, Orlando A, et al. Our recommendations for acute management of COVID-19. *Crit Care*. 2020 May 8;24(1):207. [Full text](#) [Abstract](#)
528. Centre for Evidence-Based Medicine; Jones L, Candy B, Roberts N, et al. How can healthcare workers adapt non-pharmacological treatment – whilst maintaining safety – when treating people with COVID-19 and delirium? 2020 [internet publication]. [Full text](#)
529. Public Health England. Mouth care for hospitalised patients with confirmed or suspected COVID-19. 2020 [internet publication]. [Full text](#)
530. Barnes GD, Burnett A, Allen A, et al. Thromboembolism and anticoagulant therapy during the COVID-19 pandemic: interim clinical guidance from the Anticoagulation Forum. *J Thromb Thrombolysis*. 2020 May 21 [Epub ahead of print]. [Full text](#) [Abstract](#)
531. Moores LK, Tritschler T, Brosnahan S, et al. Prevention, diagnosis, and treatment of VTE in patients with coronavirus disease 2019: CHEST guideline and expert panel report. *Chest*. 2020 Jun 2 [Epub ahead of print]. [Full text](#) [Abstract](#)
532. American Society Of Hematology. COVID-19 and VTE/anticoagulation: frequently asked questions. 2020 [internet publication]. [Full text](#)
533. Bikdeli B, Madhavan MV, Jimenez D, et al. COVID-19 and thrombotic or thromboembolic disease: implications for prevention, antithrombotic therapy, and follow-up. *J Am Coll Cardiol*. 2020 Apr 15 [Epub ahead of print]. [Full text](#) [Abstract](#)
534. Nadkarni GN, Lala A, Bagiella E, et al. Anticoagulation, mortality, bleeding and pathology among patients hospitalized with COVID-19: a single health system study. *J Am Coll Cardiol*. 2020 Aug 24 [Epub ahead of print]. [Full text](#) [Abstract](#)
535. WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group; Sterne JAC, Murthy S, Diaz JV, et al. Association between administration of systemic corticosteroids and mortality among critically ill patients with COVID-19: a meta-analysis. *JAMA*. 2020 Sep 2 [Epub ahead of print]. [Full text](#) [Abstract](#)
536. Lamontagne F, Agoritsas T, Macdonald H, et al. A living WHO guideline on drugs for covid-19. *BMJ*. 2020 Sep 4;370:m3379. [Full text](#) [Abstract](#)

537. European Medicines Agency. EMA endorses use of dexamethasone in COVID-19 patients on oxygen or mechanical ventilation. 2020 [internet publication]. [Full text](#)
538. European Medicines Agency. First COVID-19 treatment recommended for EU authorisation. 2020 [internet publication]. [Full text](#)
539. US Food and Drug Administration. COVID-19 update: FDA broadens emergency use authorization for veklury (remdesivir) to include all hospitalized patients for treatment of COVID-19. 2020 [internet publication]. [Full text](#)
540. Rochwerg B, Agarwal A, Zeng L, et al. Remdesivir for severe covid-19: a clinical practice guideline. *BMJ*. 2020 Jul 30;370:m2924. [Full text](#) [Abstract](#)
541. National Institute for Health and Care Excellence. COVID 19 rapid evidence summary: remdesivir for treating hospitalised patients with suspected or confirmed COVID-19. 2020 [internet publication]. [Full text](#)
542. Canelli R, Connor CW, Gonzalez M, et al. Barrier enclosure during endotracheal intubation. *N Engl J Med*. 2020 May 14;382(20):1957-8. [Full text](#) [Abstract](#)
543. Matava CT, Yu J, Denning S. Clear plastic drapes may be effective at limiting aerosolization and droplet spray during extubation: implications for COVID-19. *Can J Anaesth*. 2020 Apr 3 [Epub ahead of print]. [Full text](#) [Abstract](#)
544. Lucchini A, Giani M, Isgrò S, et al. The "helmet bundle" in COVID-19 patients undergoing non invasive ventilation. *Intensive Crit Care Nurs*. 2020 Apr 2:102859. [Full text](#) [Abstract](#)
545. Adir Y, Segol O, Kompaniets D, et al. Covid19: minimising risk to healthcare workers during aerosol producing respiratory therapy using an innovative constant flow canopy. *Eur Respir J*. 2020 Apr 20 [Epub ahead of print]. [Full text](#) [Abstract](#)
546. McEnery T, Gough C, Costello RW. COVID-19: respiratory support outside the intensive care unit. *Lancet Respir Med*. 2020 Apr 9 [Epub ahead of print]. [Full text](#) [Abstract](#)
547. NHS England. Guidance for the role and use of non-invasive respiratory support in adult patients with COVID19 (confirmed or suspected). 2020 [internet publication]. [Full text](#)
548. Li J, Fink JB, Ehrmann S. High-flow nasal cannula for COVID-19 patients: low risk of bio-aerosol dispersion. *Eur Respir J*. 2020 May 14;55(5):2000892. [Full text](#) [Abstract](#)
549. Schünemann HJ, Khabsa J, Solo K, et al. Ventilation techniques and risk for transmission of coronavirus disease, including COVID-19. *Ann Intern Med*. 2020 May 22 [Epub ahead of print]. [Full text](#) [Abstract](#)
550. Mahase E. Covid-19: most patients require mechanical ventilation in first 24 hours of critical care. *BMJ*. 2020 Mar 24;368:m1201. [Full text](#) [Abstract](#)

551. Cummings MJ, Baldwin MR, Abrams D, et al. Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study. *Lancet*. 2020 Jun 6;395(10239):1763-70. [Full text](#) [Abstract](#)
552. NHS England. Clinical guide for the management of critical care for adults with COVID-19 during the coronavirus pandemic. 2020 [internet publication]. [Full text](#)
553. Gattinoni L, Coppola S, Cressoni M, et al. Covid-19 does not lead to a "typical" acute respiratory distress syndrome. *Am J Respir Crit Care Med*. 2020 May 15;201(10):1299-300. [Full text](#) [Abstract](#)
554. Gattinoni L, Chiumello D, Rossi S. COVID-19 pneumonia: ARDS or not? *Crit Care*. 2020 Apr 16;24(1):154. [Full text](#) [Abstract](#)
555. Gattinoni L, Chiumello D, Caironi P, et al. COVID-19 pneumonia: different respiratory treatments for different phenotypes? *Intensive Care Med*. 2020 Apr 14 [Epub ahead of print]. [Full text](#) [Abstract](#)
556. Marini JJ, Gattinoni L. Management of COVID-19 respiratory distress. *JAMA*. 2020 Apr 24 [Epub ahead of print]. [Full text](#) [Abstract](#)
557. Rello J, Storti E, Belliato M, et al. Clinical phenotypes of SARS-CoV-2: implications for clinicians and researchers. *Eur Respir J*. 2020 Apr 27 [Epub ahead of print]. [Full text](#) [Abstract](#)
558. Tsolaki V, Siempos I, Magira E, et al. PEEP levels in COVID-19 pneumonia. *Crit Care*. 2020 Jun 6;24(1):303. [Full text](#) [Abstract](#)
559. Bos LD, Paulus F, Vlaar APJ, et al. Subphenotyping ARDS in COVID-19 patients: consequences for ventilator management. *Ann Am Thorac Soc*. 2020 May 12 [Epub ahead of print]. [Full text](#) [Abstract](#)
560. Jain A, Doyle DJ. Stages or phenotypes? A critical look at COVID-19 pathophysiology. *Intensive Care Med*. 2020 May 18;:1-2. [Full text](#) [Abstract](#)
561. Rice TW, Janz DR. In defense of evidence-based medicine for the treatment of COVID-19 ARDS. *Ann Am Thorac Soc*. 2020 Apr 22 [Epub ahead of print]. [Full text](#) [Abstract](#)
562. Carsetti A, Damia Paciarini A, Marini B, et al. Prolonged prone position ventilation for SARS-CoV-2 patients is feasible and effective. *Crit Care*. 2020 May 15;24(1):225. [Full text](#) [Abstract](#)
563. Pan C, Chen L, Lu C, et al. Lung recruitability in SARS-CoV-2 associated acute respiratory distress syndrome: a single-center, observational study. *Am J Respir Crit Care Med*. 2020 May 15;201(10):1294-7. [Full text](#) [Abstract](#)
564. Sartini C, Tresoldi M, Scarpellini P, et al. Respiratory parameters in patients with COVID-19 after using noninvasive ventilation in the prone position outside the intensive care unit. *JAMA*. 2020 May 15 [Epub ahead of print]. [Full text](#) [Abstract](#)
565. Elharrar X, Trigui Y, Dols AM, et al. Use of prone positioning in nonintubated patients with COVID-19 and hypoxemic acute respiratory failure. *JAMA*. 2020 May 15 [Epub ahead of print]. [Full text](#) [Abstract](#)

566. American Thoracic Society; Wilson KC, Chotirmall SH, Bai C, et al. COVID-19: interim guidance on management pending empirical evidence. 2020 [internet publication]. [Full text](#)
567. Ramanathan K, Antognini D, Combes A, et al. Planning and provision of ECMO services for severe ARDS during the COVID-19 pandemic and other outbreaks of emerging infectious diseases. *Lancet Respir Med*. 2020 May;8(5):518-26. [Full text](#) [Abstract](#)
568. NHS England. Clinical guide for extra corporeal membrane oxygenation (ECMO) for respiratory failure in adults during the coronavirus pandemic. 2020 [internet publication]. [Full text](#)
569. Zeng Y, Cai Z, Xianyu Y, et al. Prognosis when using extracorporeal membrane oxygenation (ECMO) for critically ill COVID-19 patients in China: a retrospective case series. *Crit Care*. 2020 Apr 15;24(1):148. [Full text](#) [Abstract](#)
570. Jacobs JP, Stammers AH, St Louis J, et al. Extracorporeal membrane oxygenation in the treatment of severe pulmonary and cardiac compromise in COVID-19: experience with 32 patients. *ASAIO J*. 2020 Apr 17 [Epub ahead of print]. [Full text](#) [Abstract](#)
571. Schmidt M, Hajage D, Lebreton G, et al. Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome associated with COVID-19: a retrospective cohort study. *Lancet Respir Med*. 2020 Aug 13 [Epub ahead of print]. [Full text](#) [Abstract](#)
572. Mustafa AK, Alexander PJ, Joshi DJ, et al. Extracorporeal membrane oxygenation for patients with COVID-19 in severe respiratory failure. *JAMA Surg*. 2020 Aug 11 [Epub ahead of print]. [Full text](#) [Abstract](#)
573. Chen L, Jiang H, Zhao Y. Pregnancy with Covid-19: management considerations for care of severe and critically ill cases. *Am J Reprod Immunol*. 2020 Jul 4:e13299. [Full text](#) [Abstract](#)
574. Campbell KH, Tornatore JM, Lawrence KE, et al. Prevalence of SARS-CoV-2 among patients admitted for childbirth in Southern Connecticut. *JAMA*. 2020 May 26 [Epub ahead of print]. [Full text](#) [Abstract](#)
575. Fassett MJ, Lurvey LD, Yasumura L, et al. Universal SARS-Cov-2 screening in women admitted for delivery in a large managed care organization. *Am J Perinatol*. 2020 Jul 3 [Epub ahead of print]. [Full text](#) [Abstract](#)
576. Bianco A, Buckley AB, Overbey J, et al. Testing of patients and support persons for coronavirus disease 2019 (COVID-19) infection before scheduled deliveries. *Obstet Gynecol*. 2020 May 19 [Epub ahead of print]. [Full text](#) [Abstract](#)
577. Sutton D, Fuchs K, D'Alton M, et al. Universal screening for SARS-CoV-2 in women admitted for delivery. *N Engl J Med*. 2020 Apr 13 [Epub ahead of print]. [Full text](#) [Abstract](#)
578. American College of Obstetricians and Gynecologists. Novel coronavirus 2019 (COVID-19). 2020 [internet publication]. [Full text](#)
579. Favre G, Pomar L, Qi X, et al. Guidelines for pregnant women with suspected SARS-CoV-2 infection. *Lancet Infect Dis*. 2020 Mar 3 [Epub ahead of print]. [Full text](#) [Abstract](#)

580. Chen D, Yang H, Cao Y, et al. Expert consensus for managing pregnant women and neonates born to mothers with suspected or confirmed novel coronavirus (COVID-19) infection. *Int J Gynaecol Obstet.* 2020 May;149(2):130-6. [Abstract](#)
581. Royal College of Obstetricians and Gynaecologists. Coronavirus (COVID-19) infection in pregnancy: information for healthcare professionals. 2020 [internet publication]. [Full text](#)
582. American Academy of Pediatrics. Management of infants born to mothers with suspected or confirmed COVID-19. 2020 [internet publication]. [Full text](#)
583. World Health Organization. Breastfeeding and COVID-19: scientific brief. 2020 [internet publication]. [Full text](#)
584. Centers for Disease Control and Prevention. Evaluation and management considerations for neonates at risk for COVID-19. 2020 [internet publication]. [Full text](#)
585. Centers for Disease Control and Prevention. Coronavirus disease 2019 (COVID-19): care for breastfeeding women. 2020 [internet publication]. [Full text](#)
586. Kalil AC. Treating COVID-19: off-label drug use, compassionate use, and randomized clinical trials during pandemics. *JAMA* Mar 24 [Epub ahead of print]. [Full text](#) [Abstract](#)
587. Marzolini C, Battegay M, Sendi P, et al. Prescribing in COVID-19 patients: should we take into account inflammation? *Br J Clin Pharmacol.* 2020 Aug 20 [Epub ahead of print]. [Full text](#) [Abstract](#)
588. US Food and Drug Administration. FDA issues emergency use authorization for convalescent plasma as potential promising COVID-19 treatment, another achievement in administration's fight against pandemic. 2020 [internet publication]. [Full text](#)
589. Joyner MJ, Senefeld JW, Klassen SA, et al; medRxiv. Effect of convalescent plasma on mortality among hospitalized patients with COVID-19: initial three-month experience. 2020 [internet publication]. [Full text](#)
590. Sarkar S, Soni KD, Khanna P. Convalescent plasma a clutch at straws in COVID-19 management! A systematic review and meta-analysis. *J Med Virol.* 2020 Aug 10 [Epub ahead of print]. [Full text](#) [Abstract](#)
591. Piechotta V, Chai KL, Valk SJ, et al. Convalescent plasma or hyperimmune immunoglobulin for people with COVID-19: a living systematic review. *Cochrane Database Syst Rev.* 2020 Jul 10;7:CD013600. [Full text](#) [Abstract](#)
592. Wang M, Cao R, Zhang L, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. *Cell Res.* 2020 Mar;30(3):269-71. [Full text](#) [Abstract](#)
593. Cortegiani A, Ingoglia G, Ippolito M, et al. A systematic review on the efficacy and safety of chloroquine for the treatment of COVID-19. *J Crit Care.* 2020 Jun;57:279-83. [Full text](#) [Abstract](#)

594. Gautret P, Lagier JC, Parola P, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. *Int J Antimicrob Agents*. 2020 Mar 20;105949. [Full text](#) [Abstract](#)
595. Chen Z, Hu J, Zhang Z, et al; medRxiv. Efficacy of hydroxychloroquine in patients with COVID-19: results of a randomized clinical trial. 2020 [internet publication]. [Full text](#)
596. Tang W, Cao Z, Han M, et al. Hydroxychloroquine in patients with mainly mild to moderate coronavirus disease 2019: open label, randomised controlled trial. *BMJ*. 2020 May 14;369:m1849. [Full text](#) [Abstract](#)
597. Hernandez AV, Roman YM, Pasupuleti V, et al. Hydroxychloroquine or chloroquine for treatment or prophylaxis of COVID-19: a living systematic review. *Ann Intern Med*. 2020 May 27 [Epub ahead of print]. [Full text](#) [Abstract](#)
598. Hernandez AV, Roman YM, Pasupuleti V, et al. Update alert 2: hydroxychloroquine or chloroquine for the treatment or prophylaxis of COVID-19. *Ann Intern Med*. 2020 Aug 27 [Epub ahead of print]. [Full text](#) [Abstract](#)
599. Pathak DSK, Salunke DAA, Thivari DP, et al. No benefit of hydroxychloroquine in COVID-19: results of systematic review and meta-analysis of randomized controlled trials. *Diabetes Metab Syndr*. 2020 Sep 1;14(6):1673-80. [Full text](#) [Abstract](#)
600. Torjesen I. Covid-19: hydroxychloroquine does not benefit hospitalised patients, UK trial finds. *BMJ*. 2020 Jun 8;369:m2263. [Full text](#) [Abstract](#)
601. Roden DM, Harrington RA, Poppas A, et al. Considerations for drug interactions on QTc in exploratory COVID-19 (coronavirus disease 2019) treatment. *Circulation*. 2020 Jun 16;141(24):e906-7. [Full text](#) [Abstract](#)
602. Kamp TJ, Hamdan MH, January CT. Chloroquine or hydroxychloroquine for COVID-19: is cardiotoxicity a concern? *J Am Heart Assoc*. 2020 May 28:e016887. [Full text](#) [Abstract](#)
603. Bessière F, Rocchia H, Delinière A, et al. Assessment of QT intervals in a case series of patients with coronavirus disease 2019 (COVID-19) infection treated with hydroxychloroquine alone or in combination with azithromycin in an intensive care unit. *JAMA Cardiol*. 2020 May 1 [Epub ahead of print]. [Full text](#) [Abstract](#)
604. Mercurio NJ, Yen CF, Shim DJ, et al. Risk of QT interval prolongation associated with use of hydroxychloroquine with or without concomitant azithromycin among hospitalized patients testing positive for coronavirus disease 2019 (COVID-19). *JAMA Cardiol*. 2020 May 1 [Epub ahead of print]. [Full text](#) [Abstract](#)
605. Nguyen LS, Dolladille C, Drici MD, et al. Cardiovascular toxicities associated with hydroxychloroquine and azithromycin: an analysis of the World Health Organization pharmacovigilance database. *Circulation*. 2020 May 22 [Epub ahead of print]. [Full text](#) [Abstract](#)
606. Young BE, Ong SWX, Kalimuddin S, et al. Epidemiologic features and clinical course of patients infected with SARS-CoV-2 in Singapore. *JAMA*. 2020 Mar 3;323(15):1488-94. [Full text](#) [Abstract](#)

607. Cao B, Wang Y, Wen D, et al. A trial of lopinavir–ritonavir in adults hospitalized with severe COVID-19. *N Engl J Med*. 2020 May 7;382(19):1787-99. [Full text](#) [Abstract](#)
608. RECOVERY Trial. No clinical benefit from use of lopinavir-ritonavir in hospitalised COVID-19 patients studied in RECOVERY. 2020 [internet publication]. [Full text](#)
609. World Health Organization. “Solidarity” clinical trial for COVID-19 treatments. 2020 [internet publication]. [Full text](#)
610. Beyls C, Martin N, Hermida A, et al. Lopinavir-ritonavir treatment for COVID-19 infection in intensive care unit: risk of bradycardia. *Circ Arrhythm Electrophysiol*. 2020 Aug;13(8):e008798. [Full text](#) [Abstract](#)
611. Jawhara S. Could intravenous immunoglobulin collected from recovered coronavirus patients protect against COVID-19 and strengthen the immune system of new patients? *Int J Mol Sci*. 2020 Mar 25;21(7). [Full text](#) [Abstract](#)
612. Xie Y, Cao S, Li Q, et al. Effect of regular intravenous immunoglobulin therapy on prognosis of severe pneumonia in patients with COVID-19. *J Infect*. 2020 Apr 10 [Epub ahead of print]. [Full text](#) [Abstract](#)
613. Zhang J, Yang Y, Yang N, et al. Effectiveness of intravenous immunoglobulin for children with severe COVID-19: a rapid review. *Ann Transl Med*. 2020 May;8(10):625. [Full text](#) [Abstract](#)
614. Marovich M, Mascola JR, Cohen MS. Monoclonal antibodies for prevention and treatment of COVID-19. *JAMA*. 2020 Jun 15 [Epub ahead of print]. [Full text](#) [Abstract](#)
615. Eli Lilly and Company. Lilly announces start of a phase 1 study for its second potential COVID-19 antibody treatment. 2020 [internet publication]. [Full text](#)
616. Eli Lilly and Company. Lilly begins world's first study of a potential COVID-19 antibody treatment in humans. 2020 [internet publication]. [Full text](#)
617. Regeneron. Regeneron announces important advances in novel COVID-19 antibody program. 2020 [internet publication]. [Full text](#)
618. Mahase E. Covid-19: RECOVERY trial will evaluate "antiviral antibody cocktail". *BMJ*. 2020 Sep 15;370:m3584. [Full text](#) [Abstract](#)
619. Aziz M, Haghbin H, Sitta EA, et al. Efficacy of tocilizumab in COVID-19: a systematic review and meta-analysis. *J Med Virol*. 2020 Sep 12 [Epub ahead of print]. [Full text](#) [Abstract](#)
620. Genentech. Genentech’s phase III EMPACTA study showed Actemra reduced the likelihood of needing mechanical ventilation in hospitalized patients with COVID-19 associated pneumonia. 2020 [internet publication]. [Full text](#)
621. Furlow B. COVACTA trial raises questions about tocilizumab's benefit in COVID-19. *Lancet Rheumatol*. 2020 Sep 9 [Epub ahead of print]. [Full text](#) [Abstract](#)

622. Cavalli G, De Luca G, Campochiaro C, et al. Interleukin-1 blockade with high-dose anakinra in patients with COVID-19, acute respiratory distress syndrome, and hyperinflammation: a retrospective cohort study. *Lancet Rheumatol*. 2020 Jun;2(6):e325-31. [Full text](#) [Abstract](#)
623. Huet T, Beaussier H, Voisin O, et al. Anakinra for severe forms of COVID-19: a cohort study. *Lancet Rheumatol*. 2020 Jul;2(7):e393-400. [Full text](#) [Abstract](#)
624. Navarro-Millán I, Sattui SE, Lakhanpal A, et al. Use of anakinra to prevent mechanical ventilation in severe COVID-19: a case series. *Arthritis Rheumatol*. 2020 Jun 30 [Epub ahead of print]. [Full text](#) [Abstract](#)
625. National Institute for Health and Care Excellence. COVID 19 rapid evidence summary: anakinra for COVID-19 associated secondary haemophagocytic lymphohistiocytosis. 2020 [internet publication]. [Full text](#)
626. De Luca G, Cavalli G, Campochiaro C, et al. GM-CSF blockade with mavrilimumab in severe COVID-19 pneumonia and systemic hyperinflammation: a single-centre, prospective cohort study. *Lancet Rheumatol*. 2020 Aug;2(8):e465-73. [Full text](#) [Abstract](#)
627. Temesgen Z, Assi M, Shweta FNU, et al. GM-CSF neutralization with lenzilumab in severe COVID-19 pneumonia: a case-control study. *Mayo Clin Proc*. 2020 Aug [Epub ahead of print]. [Full text](#)
628. Temesgen Z, Assi M, Vergidis P, et al. First clinical use of lenzilumab to neutralize GM-CSF in patients with severe COVID-19 pneumonia. *medRxiv*. 2020 Jun 14 [Epub ahead of print]. [Full text](#) [Abstract](#)
629. Wu D, Yang XO. TH17 responses in cytokine storm of COVID-19: an emerging target of JAK2 inhibitor Fedratinib. *J Microbiol Immunol Infect*. 2020 Jun;53(3):368-70. [Full text](#) [Abstract](#)
630. Cao Y, Wei J, Zou L, et al. Ruxolitinib in treatment of severe coronavirus disease 2019 (COVID-19): a multicenter, single-blind, randomized controlled trial. *J Allergy Clin Immunol*. 2020 Jul;146(1):137-46. [Full text](#) [Abstract](#)
631. Titanji BK, Farley MM, Mehta A, et al. Use of baricitinib in patients with moderate and severe COVID-19. *Clin Infect Dis*. 2020 Jun 29 [Epub ahead of print]. [Full text](#) [Abstract](#)
632. Eli Lilly and Company. Baricitinib in combination with remdesivir reduces time to recovery in hospitalized patients with COVID-19 in NIAID-sponsored ACTT-2 trial. 2020 [internet publication]. [Full text](#)
633. ClinicalTrials.gov. Mesenchymal stem cell treatment for pneumonia patients infected with 2019 novel coronavirus. 2020 [internet publication]. [Full text](#)
634. Cheng LL, Guan WJ, Duan CY, et al. Effect of recombinant human granulocyte colony-stimulating factor for patients with coronavirus disease 2019 (COVID-19) and lymphopenia: a randomized clinical trial. *JAMA Intern Med*. 2020 Sep 10 [Epub ahead of print]. [Full text](#) [Abstract](#)
635. Centre for Evidence-Based Medicine; Soliman R, Brassey J, Plüddemann A, et al. Does BCG vaccination protect against acute respiratory infections and COVID-19? A rapid review of current evidence. 2020 [internet publication]. [Full text](#)

636. World Health Organization. Bacille Calmette-Guérin (BCG) vaccination and COVID-19: scientific brief. 2020 [internet publication]. [Full text](#)
637. Department of Health and Social Care. COVID-19 treatments could be fast-tracked through new national clinical trial initiative. 2020 [internet publication]. [Full text](#)
638. Gurwitz D. Angiotensin receptor blockers as tentative SARS-CoV-2 therapeutics. *Drug Dev Res*. 2020 Mar 4 [Epub ahead of print]. [Full text](#) [Abstract](#)
639. ClinicalTrials.gov. Losartan for patients with COVID-19 requiring hospitalization. 2020 [internet publication]. [Full text](#)
640. ClinicalTrials.gov. Losartan for patients with COVID-19 not requiring hospitalization. 2020 [internet publication]. [Full text](#)
641. Chinese Clinical Trial Registry. A randomized, open-label, blank-controlled trial for the efficacy and safety of lopinavir-ritonavir and interferon-alpha 2b in hospitalization patients with 2019-nCoV pneumonia (novel coronavirus pneumonia, NCP). 2020 [internet publication]. [Full text](#)
642. Chinese Clinical Trial Registry. Clinical study for safety and efficacy of favipiravir in the treatment of novel coronavirus pneumonia (COVID-19). 2020 [internet publication]. [Full text](#)
643. Chinese Clinical Trial Registry. Clinical study of arbidol hydrochloride tablets in the treatment of novel coronavirus pneumonia (COVID-19). 2020 [internet publication]. [Full text](#)
644. Chinese Clinical Trial Registry. Randomized, open-label, controlled trial for evaluating of the efficacy and safety of baloxavir marboxil, favipiravir, and lopinavir-ritonavir in the treatment of novel coronavirus pneumonia (COVID-19) patients. 2020 [internet publication]. [Full text](#)
645. Zeng YM, Xu XL, He XQ, et al. Comparative effectiveness and safety of ribavirin plus interferon-alpha, lopinavir/ritonavir plus interferon-alpha and ribavirin plus lopinavir/ritonavir plus interferon-alpha in patients with mild to moderate novel coronavirus pneumonia. *Chin Med J (Engl)*. 2020 May 5;133(9):1132-4. [Full text](#) [Abstract](#)
646. Li H, Wang YM, Xu JY, et al. Potential antiviral therapeutics for 2019 novel coronavirus [in Chinese]. *Zhonghua Jie He He Hu Xi Za Zhi*. 2020 Mar 12;43(3):170-2. [Abstract](#)
647. Deng L, Li C, Zeng Q, et al. Arbidol combined with LPV/r versus LPV/r alone against corona virus disease 2019: a retrospective cohort study. *J Infect*. 2020 Jul;81(1):e1-5. [Full text](#) [Abstract](#)
648. ClinicalTrials.gov. Efficacy and safety of darunavir and cobicistat for treatment of pneumonia caused by 2019-nCoV (DACO-nCoV). 2020 [internet publication]. [Full text](#)
649. Synairgen. COVID-19. 2020 [internet publication]. [Full text](#)
650. CytoDyn Inc. Leronlimab used in seven patients with severe COVID-19 demonstrated promise with two intubated patients in ICU, removed from ICU and extubated with reduced pulmonary inflammation. 2020 [internet publication]. [Full text](#)

651. Huang D, Yu H, Wang T, et al. Efficacy and safety of umifenovir for coronavirus disease 2019 (COVID-19): a systematic review and meta-analysis. *J Med Virol*. 2020 Jul 3 [Epub ahead of print]. [Full text](#) [Abstract](#)
652. Hung IF, Lung KC, Tso EY, et al. Triple combination of interferon beta-1b, lopinavir-ritonavir, and ribavirin in the treatment of patients admitted to hospital with COVID-19: an open-label, randomised, phase 2 trial. *Lancet*. 2020 May 30;395(10238):1695-704. [Full text](#) [Abstract](#)
653. National Institutes of Health. NIH clinical trial testing remdesivir plus interferon beta-1a for COVID-19 treatment begins. 2020 [internet publication]. [Full text](#)
654. University of Oxford. PRINCIPLE trial. 2020 [internet publication]. [Full text](#)
655. Caly L, Druce JD, Catton MG, et al. The FDA-approved drug ivermectin inhibits the replication of SARS-CoV-2 in vitro. *Antiviral Res*. 2020 Jun;178:104787. [Full text](#) [Abstract](#)
656. Momekov G, Momekova D; medRxiv. Ivermectin as a potential COVID-19 treatment from the pharmacokinetic point of view: antiviral levels are not likely attainable with known dosing regimens. 2020 [internet publication]. [Full text](#)
657. Boretti A, Banik BK. Intravenous vitamin C for reduction of cytokines storm in acute respiratory distress syndrome. *PharmaNutrition*. 2020 Apr 21:100190. [Full text](#) [Abstract](#)
658. ClinicalTrials.gov. Vitamin C infusion for the treatment of severe 2019-nCoV infected pneumonia. 2020 [internet publication]. [Full text](#)
659. Baladia E, Pizarro AB, Ortiz-Muñoz L, et al. Vitamin C for COVID-19: a living systematic review. *Medwave*. 2020 Jul 28;20(6):e7978. [Full text](#) [Abstract](#)
660. Grant WB, Lahore H, McDonnell SL, et al. Evidence that vitamin D supplementation could reduce risk of influenza and COVID-19 infections and deaths. *Nutrients*. 2020 Apr 2;12(4). [Full text](#) [Abstract](#)
661. McCartney DM, Byrne DG. Optimisation of vitamin D status for enhanced immuno-protection against Covid-19. *Ir Med J*. 2020 Apr 3;113(4):58. [Full text](#) [Abstract](#)
662. Jakovac H. COVID-19 and vitamin D: is there a link and an opportunity for intervention? *Am J Physiol Endocrinol Metab*. 2020 May 1;318(5):E589. [Full text](#) [Abstract](#)
663. ClinicalTrials.gov. Vitamin D on prevention and treatment of COVID-19 (COVITD-19). 2020 [internet publication]. [Full text](#)
664. ClinicalTrials.gov. COVID-19 and vitamin D supplementation: a multicenter randomized controlled trial of high dose versus standard dose vitamin D3 in high-risk COVID-19 patients (CoVitTrial). 2020 [internet publication]. [Full text](#)
665. Centre for Evidence-Based Medicine; Lee J, van Hecke O, Roberts N. Vitamin D: a rapid review of the evidence for treatment or prevention in COVID-19. 2020 [internet publication]. [Full text](#)
666. Castillo ME, Entrenas Costa LM, Vaquero Barrios JM, et al. Effect of calcifediol treatment and best available therapy versus best available therapy on intensive care unit admission and mortality among

patients hospitalized for COVID-19: a pilot randomized clinical study. *J Steroid Biochem Mol Biol.* 2020 Aug 29;105751. [Full text](#) [Abstract](#)

667. National Institute for Health and Care Excellence. COVID-19 rapid evidence summary: vitamin D for COVID-19. 2020 [internet publication]. [Full text](#)
668. Mak JWY, Chan FKL, Ng SC. Probiotics and COVID-19: authors' reply. *Lancet Gastroenterol Hepatol.* 2020 Aug;5(8):722-3. [Full text](#) [Abstract](#)
669. Yang Y, Islam MS, Wang J, et al. Traditional Chinese medicine in the treatment of patients infected with 2019-new coronavirus (SARS-CoV-2): a review and perspective. *Int J Biol Sci.* 2020 Mar 15;16(10):1708-17. [Full text](#) [Abstract](#)
670. Harch PG. Hyperbaric oxygen treatment of novel coronavirus (COVID-19) respiratory failure. *Med Gas Res.* Apr-Jun 2020;10(2):61-2. [Abstract](#)
671. Thibodeaux K, Speyrer M, Raza A, et al. Hyperbaric oxygen therapy in preventing mechanical ventilation in COVID-19 patients: a retrospective case series. *J Wound Care.* 2020 May 1;29(sup5a):S4-8. [Abstract](#)
672. ClinicalTrials.gov. Hyperbaric oxygen for COVID-19 patients. 2020 [internet publication]. [Full text](#)
673. ClinicalTrials.gov. Safety and efficacy of hyperbaric oxygen for ARDS in patients with COVID-19 (COVID-19-HBO). 2020 [internet publication]. [Full text](#)
674. Martel J, Ko YF, Young JD, et al. Could nasal nitric oxide help to mitigate the severity of COVID-19? *Microbes Infect.* 2020 May 6 [Epub ahead of print]. [Full text](#) [Abstract](#)
675. ClinicalTrials.gov. Intravenous aviptadil for critical COVID-19 with respiratory failure (COVID-AIV). 2020 [internet publication]. [Full text](#)
676. ClinicalTrials.gov. Inhaled aviptadil for the treatment of non-acute lung injury in COVID-19 (AVINALI). 2020 [internet publication]. [Full text](#)
677. NeuroRx. NeuroRx submits request for emergency use authorization for RLF-100™ (aviptadil) in the treatment of patients with critical COVID-19 and respiratory failure who have exhausted approved therapy. 2020 [internet publication]. [Full text](#)
678. van de Veerdonk FL, Kouijzer IJE, de Nooijer AH, et al. Outcomes associated with use of a kinin B2 receptor antagonist among patients with COVID-19. *JAMA Netw Open.* 2020 Aug 3;3(8):e2017708. [Full text](#) [Abstract](#)
679. Vanda Pharmaceuticals Inc. Vanda Pharmaceuticals' interim analysis from ODYSSEY study shows tradipitant may accelerate clinical improvement in patients with COVID-19 pneumonia. 2020 [internet publication]. [Full text](#)
680. ClinicalTrials.gov. ODYSSEY: a study to investigate the efficacy of tradipitant in treating severe or critical COVID-19 infection. 2020 [internet publication]. [Full text](#)

681. Centers for Disease Control and Prevention. Information for healthcare professionals about coronavirus (COVID-19). 2020 [internet publication]. [Full text](#)
682. Centers for Disease Control and Prevention. Interim clinical guidance for management of patients with confirmed coronavirus disease (COVID-19). 2020 [internet publication]. [Full text](#)
683. Centers for Disease Control and Prevention. Information for clinicians on investigational therapeutics for patients with COVID-19. 2020 [internet publication]. [Full text](#)
684. Centers for Disease Control and Prevention. Interim guidance for implementing home care of people not requiring hospitalization for coronavirus disease 2019 (COVID-19). 2020 [internet publication]. [Full text](#)
685. Centers for Disease Control and Prevention. Interim U.S. guidance for risk assessment and work restrictions for healthcare personnel with potential exposure to COVID-19. 2020 [internet publication]. [Full text](#)
686. American Academy of Pediatrics. Caring for children and youth with special health care needs during the COVID-19 pandemic. 2020 [internet publication]. [Full text](#)
687. Government of Canada. Coronavirus disease (COVID-19): outbreak update. 2020 [internet publication]. [Full text](#)
688. World Health Organization. Home care for patients with suspected or confirmed COVID-19 and management of their contacts. 2020 [internet publication]. [Full text](#)
689. World Health Organization. Criteria for releasing COVID-19 patients from isolation: scientific brief. 2020 [internet publication]. [Full text](#)
690. Liu E, Smyth RL, Luo Z, et al. Rapid advice guidelines for management of children with COVID-19. *Ann Transl Med.* 2020 May;8(10):617. [Full text](#) [Abstract](#)
691. Pan American Health Organization. COVID-19 guidance and the latest research in the Americas. 2020 [internet publication]. [Full text](#)
692. Thachil J, Tang N, Gando S, et al. ISTH interim guidance on recognition and management of coagulopathy in COVID-19. *J Thromb Haemost.* 2020 May;18(5):1023-6. [Full text](#) [Abstract](#)
693. Boelig RC, Manuck T, Oliver EA, et al. Labor and delivery guidance for COVID-19. *Am J Obstet Gynecol MFM.* 2020 May;2(2):100110. [Full text](#) [Abstract](#)
694. Poon LC, Yang H, Dumont S, et al. ISUOG interim guidance on coronavirus disease 2019 (COVID-19) during pregnancy and puerperium: information for healthcare professionals – an update. *Ultrasound Obstet Gynecol.* 2020 Jun;55(6):848-62. [Full text](#) [Abstract](#)
695. NHS England. Coronavirus specialty guides. 2020 [internet publication]. [Full text](#)
696. National Institute for Health and Care Excellence. Coronavirus (COVID-19): rapid guidelines and evidence reviews. 2020 [internet publication]. [Full text](#)

697. BMJ Publishing Group. BMJ's coronavirus (covid-19) hub. 2020 [internet publication]. [Full text](#)
698. British Thoracic Society. COVID-19: information for the respiratory community. 2020 [internet publication]. [Full text](#)
699. NHS England. After-care needs of inpatients recovering from COVID-19. 2020 [internet publication]. [Full text](#)
700. Royal College of General Practitioners; Association for Palliative Medicine. Community palliative, end of life and bereavement care in the COVID-19 pandemic. 2020 [internet publication]. [Full text](#)
701. Calvo C, García López-Hortelano M, de Carlos Vicente JC, et al; Spanish Paediatric Association working group. Recommendations on the clinical management of the COVID-19 infection by the new coronavirus SARS-CoV2 [in Spanish]. *An Pediatr (Barc)*. 2020 Apr;92(4):241. [Full text](#) [Abstract](#)
702. Shang Y, Pan C, Yang X, et al. Management of critically ill patients with COVID-19 in ICU: statement from front-line intensive care experts in Wuhan, China. *Ann Intensive Care*. 2020 Jun 6;10(1):73. [Full text](#) [Abstract](#)
703. Chinese Center for Disease Control and Prevention. Coronavirus disease. 2020 [internet publication]. [Full text](#)
704. First Affiliated Hospital, Zhejiang University School of Medicine. Handbook of COVID-19 prevention and treatment. 2020 [internet publication]. [Full text](#)
705. National Health Commission of the People's Republic of China; National Administration of Traditional Chinese Medicine of the People's Republic of China. Diagnosis and treatment protocol for novel coronavirus pneumonia (trial version 7). *Chin Med J (Engl)*. 2020 May 5;133(9):1087-95. [Full text](#) [Abstract](#)
706. Ministry of Health Singapore. Updates on COVID-19 (coronavirus disease 2019) local situation. 2020 [internet publication]. [Full text](#)
707. National Institute of Infectious Diseases Japan. New coronavirus infectious disease (COVID-19) related information page. 2020 [internet publication]. [Full text](#)
708. Japanese Association for Infectious Diseases. COVID-19 infection. 2020 [internet publication]. [Full text](#)
709. Working Group for the Prevention and Control of Neonatal SARS-CoV-2 Infection in the Perinatal Period of the Editorial Committee of Chinese Journal of Contemporary Pediatrics. Perinatal and neonatal management plan for prevention and control of SARS-CoV-2 infection (2nd edition) [in Chinese]. *Zhongguo Dang Dai Er Ke Za Zhi*. 2020 Mar;22(3):195-8. [Abstract](#)
710. Department of Health Australia. Coronavirus disease 2019 (COVID-19). 2020 [internet publication]. [Full text](#)
711. World Health Organization. Coronavirus disease (COVID-19) weekly epidemiological updates. 2020 [internet publication]. [Full text](#)

712. Verity R, Okell LC, Dorigatti I, et al. Estimates of the severity of coronavirus disease 2019: a model-based analysis. *Lancet Infect Dis*. 2020 Jun;20(6):669-77. [Full text](#) [Abstract](#)
713. Williamson EJ, Walker AJ, Bhaskaran K, et al. OpenSAFELY: factors associated with COVID-19 death in 17 million patients. *Nature*. 2020 Jul 8 [Epub ahead of print]. [Full text](#) [Abstract](#)
714. Centre for Evidence-Based Medicine; Oke J, Heneghan C. Global COVID-19 case fatality rates. 2020 [internet publication]. [Full text](#)
715. Mahase E. Covid-19: the problems with case counting. *BMJ*. 2020 Sep 3;370:m3374. [Full text](#) [Abstract](#)
716. Centre for Evidence-Based Medicine; Oke J, Heneghan C. Reconciling COVID-19 death data in the UK. 2020 [internet publication]. [Full text](#)
717. Onder G, Rezza G, Brusaferro S. Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. *JAMA*. 2020 Mar 23 [Epub ahead of print]. [Full text](#) [Abstract](#)
718. Mahase E. Coronavirus covid-19 has killed more people than SARS and MERS combined, despite lower case fatality rate. *BMJ*. 2020 Feb 18;368:m641. [Full text](#) [Abstract](#)
719. Rajgor DD, Lee MH, Archuleta S, et al. The many estimates of the COVID-19 case fatality rate. *Lancet Infect Dis*. 2020 Jul;20(7):776-7. [Full text](#) [Abstract](#)
720. Department of Health and Social Care. UK Biobank COVID-19 antibody study: round 1 results. 2020 [internet publication]. [Full text](#)
721. Department of Health & Social Care. REACT-2: real-time assessment of community transmission – prevalence of coronavirus (COVID-19) antibodies in June 2020. 2020 [internet publication]. [Full text](#)
722. Centers for Disease Control and Prevention. Commercial laboratory seroprevalence survey data. 2020 [internet publication]. [Full text](#)
723. Pollán M, Pérez-Gómez B, Pastor-Barriuso R, et al. Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study. *Lancet*. 2020 Jul 3 [Epub ahead of print]. [Full text](#) [Abstract](#)
724. Perez-Saez J, Lauer SA, Kaiser L, et al. Serology-informed estimates of SARS-CoV-2 infection fatality risk in Geneva, Switzerland. *Lancet Infect Dis*. 2020 Jul 14 [Epub ahead of print]. [Full text](#) [Abstract](#)
725. Shakiba M, Hashemi Nazari SS, Mehrabian F, et al; medRxiv. Seroprevalence of COVID-19 virus infection in Guilan province, Iran. 2020 [internet publication]. [Full text](#)
726. Erikstrup C, Hother CE, Pedersen OB, et al; medRxiv. Estimation of SARS-CoV-2 infection fatality rate by real-time antibody screening of blood donors. 2020 [internet publication]. [Full text](#)
727. Los Angeles County Department of Public Health. USC-LA county study: early results of antibody testing suggest number of COVID-19 infections far exceeds number of confirmed cases in Los Angeles County. 2020 [internet publication]. [Full text](#)

728. Sood N, Simon P, Ebner P, et al. Seroprevalence of SARS-CoV-2-specific antibodies among adults in Los Angeles County, California, on April 10-11, 2020. *JAMA*. 2020 May 18;323(23):2425-7. [Full text](#) [Abstract](#)
729. Bendavid E, Mulaney B, Sood N; medRxiv. COVID-19 antibody seroprevalence in Santa Clara County, California. 2020 [internet publication]. [Full text](#)
730. Korth J, Wilde W, Dolff S, et al. SARS-CoV-2-specific antibody detection in healthcare workers in Germany with direct contact to COVID-19 patients. *J Clin Virol*. 2020 May 13;104437. [Full text](#) [Abstract](#)
731. Gudbjartsson DF, Norddahl GL, Melsted P, et al. Humoral immune response to SARS-CoV-2 in Iceland. *N Engl J Med*. 2020 Sep 1 [Epub ahead of print]. [Full text](#) [Abstract](#)
732. Xu X, Sun J, Nie S, et al. Seroprevalence of immunoglobulin M and G antibodies against SARS-CoV-2 in China. *Nat Med*. 2020 Jun 5 [Epub ahead of print]. [Full text](#) [Abstract](#)
733. Guan WJ, Liang WH, Zhao Y, et al. Comorbidity and its impact on 1590 patients with Covid-19 in China: a nationwide analysis. *Eur Respir J*. 2020 May 14;55(5):2000547. [Full text](#) [Abstract](#)
734. Sorbello M, El-Boghdady K, Di Giacinto I, et al. The Italian COVID-19 outbreak: experiences and recommendations from clinical practice. *Anaesthesia*. 2020 Jun;75(6):724-32. [Full text](#) [Abstract](#)
735. Grasselli G, Zangrillo A, Zanella A, et al. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy Region, Italy. *JAMA*. 2020 Apr 6;323(16):1574-81. [Full text](#) [Abstract](#)
736. Arentz M, Yim E, Klaff L, et al. Characteristics and outcomes of 21 critically ill patients with COVID-19 in Washington State. *JAMA*. 2020 Mar 19;323(16):1612-4. [Full text](#) [Abstract](#)
737. McMichael TM, Currie DW, Clark S, et al. Epidemiology of Covid-19 in a long-term care facility in King County, Washington. *N Engl J Med*. 2020 May 21;382(21):2005-11. [Full text](#) [Abstract](#)
738. Mehta V, Goel S, Kabarriti R, et al. Case fatality rate of cancer patients with COVID-19 in a New York hospital system. *Cancer Discov*. 2020 Jul;10(7):935-41. [Full text](#) [Abstract](#)
739. Bixler D, Miller AD, Mattison CP, et al. SARS-CoV-2-associated deaths among persons aged <21 years: United States, February 12–July 31, 2020. *MMWR Morb Mortal Wkly Rep*. 2020 Sep 18;69(37):1324-9. [Full text](#) [Abstract](#)
740. Ruan Q, Yang K, Wang W, et al. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. *Intensive Care Med*. 2020 May;46(5):846-8. [Full text](#) [Abstract](#)
741. Hasan SS, Capstick T, Ahmed R, et al. Mortality in COVID-19 patients with acute respiratory distress syndrome and corticosteroids use: a systematic review and meta-analysis. *Expert Rev Respir Med*. 2020 Jul 31 [Epub ahead of print]. [Full text](#) [Abstract](#)

742. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. *JAMA*. 2020 Apr 22;323(20):2052-9. [Full text](#) [Abstract](#)
743. Docherty AB, Harrison EM, Green CA, et al; medRxiv. Features of 16,749 hospitalised UK patients with COVID-19 using the ISARIC WHO Clinical Characterisation Protocol. 2020 [internet publication]. [Full text](#)
744. Auld SC, Caridi-Scheible M, Blum JM, et al. ICU and ventilator mortality among critically ill adults with coronavirus disease 2019. *Crit Care Med*. 2020 May 26 [Epub ahead of print]. [Full text](#) [Abstract](#)
745. Yang F, Shi S, Zhu J, et al. Analysis of 92 deceased patients with COVID-19. *J Med Virol*. 2020 Apr 15 [Epub ahead of print]. [Full text](#) [Abstract](#)
746. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med*. 2020 May;8(5):475-81. [Full text](#) [Abstract](#)
747. Figliozzi S, Masci PG, Ahmadi N, et al. Predictors of adverse prognosis in Covid-19: a systematic review and meta-analysis. *Eur J Clin Invest*. 2020 Jul 29:e13362. [Full text](#) [Abstract](#)
748. Parohan M, Yaghoubi S, Seraji A, et al. Risk factors for mortality in patients with coronavirus disease 2019 (COVID-19) infection: a systematic review and meta-analysis of observational studies. *Aging Male*. 2020 Jun 8:1-9. [Full text](#) [Abstract](#)
749. Zou X, Li S, Fang M, et al. Acute physiology and chronic health evaluation II score as a predictor of hospital mortality in patients of coronavirus disease 2019. *Crit Care Med*. 2020 May 1;48(8):e657-65. [Full text](#) [Abstract](#)
750. Fan G, Tu C, Zhou F, et al. Comparison of severity scores for COVID-19 patients with pneumonia: a retrospective study. *Eur Respir J*. 2020 Jul 16 [Epub ahead of print]. [Full text](#) [Abstract](#)
751. Ji D, Zhang D, Xu J, et al. Prediction for progression risk in patients with COVID-19 pneumonia: the CALL score. *Clin Infect Dis*. 2020 Apr 9 [Epub ahead of print]. [Full text](#) [Abstract](#)
752. Liang W, Liang H, Ou L, et al. Development and validation of a clinical risk score to predict the occurrence of critical illness in hospitalized patients with COVID-19. *JAMA Intern Med*. 2020 May 12 [Epub ahead of print]. [Full text](#) [Abstract](#)
753. Knight SR, Ho A, Pius R, et al. Risk stratification of patients admitted to hospital with covid-19 using the ISARIC WHO clinical characterisation protocol: development and validation of the 4C mortality score. *BMJ*. 2020 Sep 9;370:m3339. [Full text](#) [Abstract](#)
754. Mo P, Xing Y, Xiao Y, et al. Clinical characteristics of refractory COVID-19 pneumonia in Wuhan, China. *Clin Infect Dis*. 2020 Mar 16 [Epub ahead of print]. [Full text](#) [Abstract](#)
755. Chen D, Xu W, Lei Z, et al. Recurrence of positive SARS-CoV-2 RNA in COVID-19: a case report. *Int J Infect Dis*. 2020 Mar 5;93:297-9. [Full text](#) [Abstract](#)

756. Xing Y, Mo P, Xiao Y, et al. Post-discharge surveillance and positive virus detection in two medical staff recovered from coronavirus disease 2019 (COVID-19), China, January to February 2020. *Euro Surveill.* 2020 Mar;25(10). [Full text](#) [Abstract](#)
757. Mattiuzzi C, Henry BM, Sanchis-Gomar F, et al. SARS-CoV-2 recurrent RNA positivity after recovering from coronavirus disease 2019 (COVID-19): a meta-analysis. *Acta Biomed.* 2020 Sep 7;91(3):e2020014. [Full text](#) [Abstract](#)
758. Arafkas M, Khosrawipour T, Kocbach P, et al. Current meta-analysis does not support the possibility of COVID-19 reinfections. *J Med Virol.* 2020 Sep 8 [Epub ahead of print]. [Abstract](#)
759. Parry J. Covid-19: Hong Kong scientists report first confirmed case of reinfection. *BMJ.* 2020 Aug 26;370:m3340. [Full text](#) [Abstract](#)
760. Chandrashekar A, Liu J, Martinot AJ, et al. SARS-CoV-2 infection protects against rechallenge in rhesus macaques. *Science.* 2020 May 20 [Epub ahead of print]. [Full text](#) [Abstract](#)
761. Kirkcaldy RD, King BA, Brooks JT. COVID-19 and postinfection immunity: limited evidence, many remaining questions. *JAMA.* 2020 May 11 [Epub ahead of print]. [Full text](#) [Abstract](#)
762. Ni L, Ye F, Cheng ML, et al. Detection of SARS-CoV-2-specific humoral and cellular immunity in COVID-19 convalescent individuals. *Immunity.* 2020 Jun 16;52(6):971-7. [Full text](#) [Abstract](#)
763. Wu F, Liu M, Wang A, et al. Evaluating the association of clinical characteristics with neutralizing antibody levels in patients who have recovered from mild COVID-19 in Shanghai, China. *JAMA Intern Med.* 2020 Aug 18 [Epub ahead of print]. [Full text](#) [Abstract](#)
764. Long QX, Tang XJ, Shi QL, et al. Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections. *Nat Med.* 2020 Jun 18 [Epub ahead of print]. [Full text](#) [Abstract](#)
765. Centre for Evidence-Based Medicine; Kernohan A, Calderon M. What are the risk factors and effectiveness of prophylaxis for venous thromboembolism in COVID-19 patients? 2020 [internet publication]. [Full text](#)
766. Lu YF, Pan LY, Zhang WW, et al. A meta-analysis of the incidence of venous thromboembolic events and impact of anticoagulation on mortality in patients with COVID-19. *Int J Infect Dis.* 2020 Aug 13 [Epub ahead of print]. [Full text](#) [Abstract](#)
767. Ranucci M, Ballotta A, Di Dedda U, et al. The procoagulant pattern of patients with COVID-19 acute respiratory distress syndrome. *J Thromb Haemost.* 2020 Jul;18(7):1747-51. [Full text](#) [Abstract](#)
768. Bilaloglu S, Aphinyanaphongs Y, Jones S, et al. Thrombosis in hospitalized patients With COVID-19 in a New York City health system. *JAMA.* 2020 Jul 20 [Epub ahead of print]. [Full text](#) [Abstract](#)
769. Levi M, Thachil J, Iba T, et al. Coagulation abnormalities and thrombosis in patients with COVID-19. *Lancet Haematol.* 2020 May 11;7(6):e438-40. [Full text](#) [Abstract](#)

770. Demelo-Rodríguez P, Cervilla-Muñoz E, Ordieres-Ortega L, et al. Incidence of asymptomatic deep vein thrombosis in patients with COVID-19 pneumonia and elevated D-dimer levels. *Thromb Res*. 2020 May 13;192:23-6. [Full text](#) [Abstract](#)
771. Wichmann D, Sperhake JP, Lütgehetmann M, et al. Autopsy findings and venous thromboembolism in patients with COVID-19: a prospective cohort study. *Ann Intern Med*. 2020 May 6 [Epub ahead of print]. [Full text](#) [Abstract](#)
772. Wang T, Chen R, Liu C, et al. Attention should be paid to venous thromboembolism prophylaxis in the management of COVID-19. *Lancet Haematol*. 2020 May;7(5):e362-3. [Full text](#) [Abstract](#)
773. Zhang Y, Xiao M, Zhang S, et al. Coagulopathy and antiphospholipid antibodies in patients with Covid-19. *N Engl J Med*. 2020 Apr 23;382(17):e38. [Full text](#) [Abstract](#)
774. Bowles L, Platton S, Yartey N, et al. Lupus anticoagulant and abnormal coagulation tests in patients with Covid-19. *N Engl J Med*. 2020 Jul 16;383(3):288-90. [Full text](#) [Abstract](#)
775. Galeano-Valle F, Oblitas CM, Ferreiro-Mazón MM, et al. Antiphospholipid antibodies are not elevated in patients with severe COVID-19 pneumonia and venous thromboembolism. *Thromb Res*. 2020 Aug;192:113-5. [Full text](#) [Abstract](#)
776. Xiao M, Zhang Y, Zhang S, et al. Brief report: anti-phospholipid antibodies in critically ill patients with coronavirus disease 2019 (COVID-19). *Arthritis Rheumatol*. 2020 Jun 30 [Epub ahead of print]. [Full text](#) [Abstract](#)
777. Reyes Gil M, Barouqa M, Szymanski J, et al. Assessment of lupus anticoagulant positivity in patients with coronavirus disease 2019 (COVID-19). *JAMA Netw Open*. 2020 Aug 3;3(8):e2017539. [Full text](#) [Abstract](#)
778. van Nieuwkoop C. COVID-19 associated pulmonary thrombosis. *Thromb Res*. 2020 Jul;191:151. [Full text](#) [Abstract](#)
779. McGonagle D, O'Donnell JS, Sharif K, et al. Immune mechanisms of pulmonary intravascular coagulopathy in COVID-19 pneumonia. *Lancet Rheumatol*. 2020 Jul;2(7):e437-45. [Full text](#) [Abstract](#)
780. Belen-Apak FB, Sarıalioğlu F. Pulmonary intravascular coagulation in COVID-19: possible pathogenesis and recommendations on anticoagulant/thrombolytic therapy. *J Thromb Thrombolysis*. 2020 Aug;50(2):278-80. [Full text](#) [Abstract](#)
781. Perini P, Nabulsi B, Massoni CB, et al. Acute limb ischaemia in two young, non-atherosclerotic patients with COVID-19. *Lancet*. 2020 May 16;395(10236):1546. [Full text](#) [Abstract](#)
782. Griffin DO, Jensen A, Khan M, et al. Arterial thromboembolic complications in COVID-19 in low-risk patients despite prophylaxis. *Br J Haematol*. 2020 Jul;190(1):e11-3. [Full text](#) [Abstract](#)
783. Lodigiani C, Iapichino G, Carenzo L, et al. Venous and arterial thromboembolic complications in COVID-19 patients admitted to an academic hospital in Milan, Italy. *Thromb Res*. 2020 Apr 23;191:9-14. [Full text](#) [Abstract](#)

784. Vulliamy P, Jacob S, Davenport RA. Acute aorto-iliac and mesenteric arterial thromboses as presenting features of COVID-19. *Br J Haematol*. 2020 Jun;189(6):1053-4. [Full text](#) [Abstract](#)
785. Hemasian H, Ansari B. First case of Covid-19 presented with cerebral venous thrombosis: a rare and dreaded case. *Rev Neurol (Paris)*. 2020 Jun;176(6):521-3. [Full text](#) [Abstract](#)
786. Madjid M, Safavi-Naeini P, Solomon SD, et al. Potential effects of coronaviruses on the cardiovascular system: a review. *JAMA Cardiol*. 2020 Mar 27 [Epub ahead of print]. [Full text](#) [Abstract](#)
787. Sala S, Peretto G, Gramegna M, et al. Acute myocarditis presenting as a reverse Tako-Tsubo syndrome in a patient with SARS-CoV-2 respiratory infection. *Eur Heart J*. 2020 May 14;41(19):1861-2. [Full text](#) [Abstract](#)
788. Liu PP, Blet A, Smyth D, et al. The science underlying COVID-19: implications for the cardiovascular system. *Circulation*. 2020 Jul 7;142(1):68-78. [Full text](#) [Abstract](#)
789. Clerkin KJ, Fried JA, Raikhelkar J, et al. Coronavirus disease 2019 (COVID-19) and cardiovascular disease. *Circulation*. 2020 May 19;141(20):1648-55. [Full text](#) [Abstract](#)
790. Hendren NS, Drazner MH, Bozkurt B, et al. Description and proposed management of the acute COVID-19 cardiovascular syndrome. *Circulation*. 2020 Jun 9;141(23):1903-14. [Full text](#) [Abstract](#)
791. Zou F, Qian Z, Wang Y, et al. Cardiac injury and COVID-19: a systematic review and meta-analysis. *CJC Open*. 2020 Jun 23 [Epub ahead of print]. [Full text](#) [Abstract](#)
792. Sabatino J, De Rosa S, Di Salvo G, et al. Impact of cardiovascular risk profile on COVID-19 outcome: a meta-analysis. *PLoS One*. 2020 Aug 14;15(8):e0237131. [Full text](#) [Abstract](#)
793. Creel-Bulos C, Hockstein M, Amin N, et al. Acute cor pulmonale in critically ill patients with Covid-19. *N Engl J Med*. 2020 May 21;382(21):e70. [Full text](#) [Abstract](#)
794. Zeng JH, Liu YX, Yuan J, et al. First case of COVID-19 complicated with fulminant myocarditis: a case report and insights. *Infection*. 2020 Apr 10;1-5. [Full text](#) [Abstract](#)
795. Inciardi RM, Lupi L, Zacccone G, et al. Cardiac involvement in a patient with coronavirus disease 2019 (COVID-19). *JAMA Cardiol*. 2020 Mar 27;5(7):1-6. [Full text](#) [Abstract](#)
796. Hua A, O'Gallagher K, Sado D, et al. Life-threatening cardiac tamponade complicating myo-pericarditis in COVID-19. *Eur Heart J*. 2020 Jun 7;41(22):2130. [Full text](#) [Abstract](#)
797. Meyer P, Degrauwe S, Delden CV, et al. Typical takotsubo syndrome triggered by SARS-CoV-2 infection. *Eur Heart J*. 2020 May 14;41(19):1860. [Full text](#) [Abstract](#)
798. Li X, Pan X, Li Y, et al. Cardiac injury associated with severe disease or ICU admission and death in hospitalized patients with COVID-19: a meta-analysis and systematic review. *Crit Care*. 2020 Jul 28;24(1):468. [Full text](#) [Abstract](#)
799. Shi S, Qin M, Shen B, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. *JAMA Cardiol*. 2020 Mar 25;5(7):802-10. [Full text](#) [Abstract](#)

800. He XW, Lai JS, Cheng J, et al. Impact of complicated myocardial injury on the clinical outcome of severe or critically ill COVID-19 patients [in Chinese]. *Zhonghua Xin Xue Guan Bing Za Zhi*. 2020 Mar 15;48(0):E011. [Abstract](#)
801. Santoso A, Pranata R, Wibowo A, et al. Cardiac injury is associated with mortality and critically ill pneumonia in COVID-19: a meta-analysis. *Am J Emerg Med*. 2020 Apr 19 [Epub ahead of print]. [Full text](#) [Abstract](#)
802. Inciardi RM, Adamo M, Lupi L, et al. Characteristics and outcomes of patients hospitalized for COVID-19 and cardiac disease in Northern Italy. *Eur Heart J*. 2020 May 14;41(19):1821-9. [Full text](#) [Abstract](#)
803. National Institute for Health and Care Excellence. COVID-19 rapid guideline: acute myocardial injury. 2020 [internet publication]. [Full text](#)
804. Siripanthong B, Nazarian S, Muser D, et al. Recognizing COVID-19-related myocarditis: the possible pathophysiology and proposed guideline for diagnosis and management. *Heart Rhythm*. 2020 May 5 [Epub ahead of print]. [Full text](#) [Abstract](#)
805. Xiong TY, Redwood S, Prendergast B, et al. Coronaviruses and the cardiovascular system: acute and long-term implications. *Eur Heart J*. 2020 May 14;41(19):1798-800. [Full text](#) [Abstract](#)
806. Puntmann VO, Carerj ML, Wieters I, et al. Outcomes of cardiovascular magnetic resonance imaging in patients recently recovered from coronavirus disease 2019 (COVID-19). *JAMA Cardiol*. 2020 Jul 27 [Epub ahead of print]. [Full text](#) [Abstract](#)
807. Fu EL, Janse RJ, de Jong Y, et al. Acute kidney injury and kidney replacement therapy in COVID-19: a systematic review and meta-analysis. *Clin Kidney J*. 2020 Sep 2;13(4):550-63. [Full text](#) [Abstract](#)
808. Stewart DJ, Hartley JC, Johnson M, et al. Renal dysfunction in hospitalised children with COVID-19. *Lancet Child Adolesc Health*. 2020 Jun 15;4(8):e28-9. [Full text](#) [Abstract](#)
809. National Institute for Health and Care Excellence. COVID-19 rapid guideline: acute kidney injury in hospital. 2020 [internet publication]. [Full text](#)
810. Farkash EA, Wilson AM, Jentzen JM. Ultrastructural evidence for direct renal infection with SARS-CoV-2. *J Am Soc Nephrol*. 2020 May 5 [Epub ahead of print]. [Full text](#) [Abstract](#)
811. Nasr SH, Kopp JB. COVID-19-associated collapsing glomerulopathy: an emerging entity. *Kidney Int Rep*. 2020 May 4;5(6):759-61. [Full text](#) [Abstract](#)
812. Gross O, Moerer O, Weber M, et al. COVID-19-associated nephritis: early warning for disease severity and complications? *Lancet*. 2020 May 16;395(10236):e87-8. [Full text](#) [Abstract](#)
813. Kunutsor SK, Laukkanen JA. Hepatic manifestations and complications of COVID-19: a systematic review and meta-analysis. *J Infect*. 2020 Jun 21 [Epub ahead of print]. [Full text](#) [Abstract](#)
814. Wijarnpreecha K, Ungprasert P, Panjawatanan P, et al. COVID-19 and liver injury: a meta-analysis. *Eur J Gastroenterol Hepatol*. 2020 Jul 3 [Epub ahead of print]. [Abstract](#)

815. Alqahtani SA, Schattenberg JM. Liver injury in COVID-19: the current evidence. *United European Gastroenterol J*. 2020 Jun;8(5):509-19. [Full text](#) [Abstract](#)
816. Wong GL, Wong VW, Thompson A, et al. Management of patients with liver derangement during the COVID-19 pandemic: an Asia-Pacific position statement. *Lancet Gastroenterol Hepatol*. 2020 Aug;5(8):776-87. [Full text](#) [Abstract](#)
817. Mao L, Jin H, Wang M, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. *JAMA Neurol*. 2020 Apr 10;77(6):1-9. [Full text](#) [Abstract](#)
818. Romero-Sánchez CM, Díaz-Maroto I, Fernández-Díaz E, et al. Neurologic manifestations in hospitalized patients with COVID-19: the ALBACOVID registry. *Neurology*. 2020 Jun 1 [Epub ahead of print]. [Full text](#) [Abstract](#)
819. Kandemirli SG, Dogan L, Sarikaya ZT, et al. Brain MRI findings in patients in the intensive care unit with COVID-19 infection. *Radiology*. 2020 May 8:201697. [Full text](#) [Abstract](#)
820. Panda PK, Sharawat IK, Panda P, et al. Neurological complications of SARS-CoV-2 infection in children: a systematic review and meta-analysis. *J Trop Pediatr*. 2020 Sep 10 [Epub ahead of print]. [Full text](#) [Abstract](#)
821. Orrù G, Conversano C, Malloggi E, et al. Neurological complications of COVID-19 and possible neuroinvasion pathways: a systematic review. *Int J Environ Res Public Health*. 2020 Sep 14;17(18):E6688. [Full text](#) [Abstract](#)
822. Restivo DA, Centonze D, Alesina A, et al. Myasthenia gravis associated with SARS-CoV-2 infection. *Ann Intern Med*. 2020 Aug 10 [Epub ahead of print]. [Full text](#) [Abstract](#)
823. Abu-Rumeileh S, Abdelhak A, Foschi M, et al. Guillain-Barré syndrome spectrum associated with COVID-19: an up-to-date systematic review of 73 cases. *J Neurol*. 2020 Aug 25 [Epub ahead of print]. [Full text](#) [Abstract](#)
824. Fridman S, Bullrich MB, Jimenez-Ruiz A, et al. Stroke risk, phenotypes, and death in COVID-19: systematic review and newly reported cases. *Neurology*. 2020 Sep 15 [Epub ahead of print]. [Full text](#) [Abstract](#)
825. Ntaios G, Michel P, Georgiopoulos G, et al. Characteristics and outcomes in patients with COVID-19 and acute ischemic stroke: the global COVID-19 stroke registry. *Stroke*. 2020 Jul 9 [Epub ahead of print]. [Full text](#) [Abstract](#)
826. Qureshi AI, Abd-Allah F, Alsenani F, et al. Management of acute ischemic stroke in patients with COVID-19 infection: report of an international panel. *Int J Stroke*. 2020 Jul;15(5):540-54. [Full text](#) [Abstract](#)
827. Lu Y, Li X, Geng D, et al. Cerebral micro-structural changes in COVID-19 patients: an MRI-based 3-month follow-up study. *EClinicalMedicine*. 2020 Aug 3 [Epub ahead of print]. [Full text](#) [Abstract](#)
828. COVID Symptom Study. How long does COVID-19 last? 2020 [internet publication]. [Full text](#)

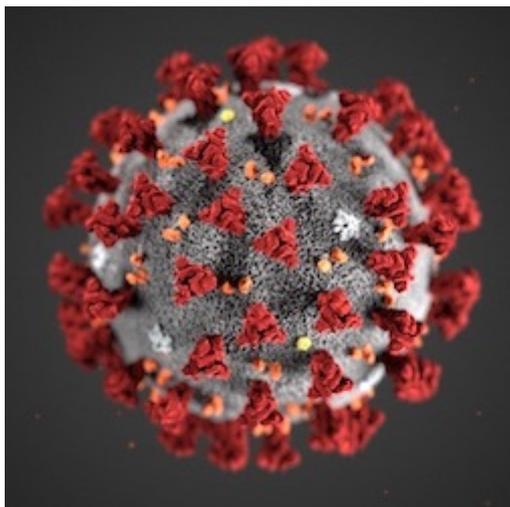
829. Mahase E. Covid-19: what do we know about “long covid”? *BMJ*. 2020 Jul 14;370:m2815. [Full text](#) [Abstract](#)
830. Carfi A, Bernabei R, Landi F, et al. Persistent symptoms in patients after acute COVID-19. *JAMA*. 2020 Jul 9 [Epub ahead of print]. [Full text](#) [Abstract](#)
831. Tenforde MW, Kim SS, Lindsell CJ, et al. Symptom duration and risk factors for delayed return to usual health among outpatients with COVID-19 in a multistate health care systems network: United States, March-June 2020. *MMWR Morb Mortal Wkly Rep*. 2020 Jul 31;69(30):993-8. [Full text](#) [Abstract](#)
832. Greenhalgh T, Knight M, A’Court C, et al. Management of post-acute covid-19 in primary care. *BMJ*. 2020 Aug 11;370:m3026. [Full text](#) [Abstract](#)
833. Rodriguez-Morales AJ, Cardona-Ospina JA, Gutiérrez-Ocampo E, et al. Clinical, laboratory and imaging features of COVID-19: a systematic review and meta-analysis. *Travel Med Infect Dis*. 2020 Mar 13:101623. [Full text](#) [Abstract](#)
834. Song JC, Wang G, Zhang W, et al. Chinese expert consensus on diagnosis and treatment of coagulation dysfunction in COVID-19. *Mil Med Res*. 2020 Apr 20;7(1):19. [Full text](#) [Abstract](#)
835. Tang N, Li D, Wang X, et al. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. *J Thromb Haemost*. 2020 Apr;18(4):844-7. [Full text](#) [Abstract](#)
836. Connors JM, Levy JH. COVID-19 and its implications for thrombosis and anticoagulation. *Blood*. 2020 Jun 4;135(23):2033-40. [Full text](#) [Abstract](#)
837. Tang N, Bai H, Chen X, et al. Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy. *J Thromb Haemost*. 2020 May;18(5):1094-9. [Full text](#) [Abstract](#)
838. Ye Q, Wang B, Mao J. The pathogenesis and treatment of the ‘cytokine storm’ in COVID-19. *J Infect*. 2020 Jun;80(6):607-13. [Full text](#) [Abstract](#)
839. Wang Z, Yang B, Li Q, et al. Clinical features of 69 cases with coronavirus disease 2019 in Wuhan, China. *Clin Infect Dis*. 2020 Mar 16 [Epub ahead of print]. [Full text](#) [Abstract](#)
840. Aziz M, Fatima R, Assaly R. Elevated interleukin-6 and severe COVID-19: a meta-analysis. *J Med Virol*. 2020 Apr 28 [Epub ahead of print]. [Full text](#) [Abstract](#)
841. Pedersen SF, Ho YC. SARS-CoV-2: a storm is raging. *J Clin Invest*. 2020 May 1;130(5):2202-5. [Full text](#) [Abstract](#)
842. Zhang W, Zhao Y, Zhang F, et al. 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. *Clin Immunol*. 2020 Mar 25:108393. [Full text](#) [Abstract](#)

843. Pain CE, Felsenstein S, Cleary G, et al. Novel paediatric presentation of COVID-19 with ARDS and cytokine storm syndrome without respiratory symptoms. *Lancet Rheumatol*. 2020 May 15;2(7):e376-9. [Full text](#) [Abstract](#)
844. Abrams JY, Godfred-Cato SE, Oster ME, et al. Multisystem inflammatory syndrome in children (MIS-C) associated with SARS-CoV-2: a systematic review. *J Pediatr*. 2020 Aug 5 [Epub ahead of print]. [Full text](#) [Abstract](#)
845. Godfred-Cato S, Bryant B, Leung J, et al. COVID-19-associated multisystem inflammatory syndrome in children: United States, March–July 2020. *MMWR Morb Mortal Wkly Rep*. 2020 Aug 14;69(32):1074-80. [Full text](#) [Abstract](#)
846. Jiang L, Tang K, Levin M, et al. COVID-19 and multisystem inflammatory syndrome in children and adolescents. *Lancet Infect Dis*. 2020 Aug 17 [Epub ahead of print]. [Full text](#) [Abstract](#)
847. Royal College of Paediatrics and Child Health. Guidance: paediatric multisystem inflammatory syndrome temporally associated with COVID-19. 2020 [internet publication]. [Full text](#)
848. Centers for Disease Control and Prevention. Multisystem inflammatory syndrome in children (MIS-C) associated with coronavirus disease 2019 (COVID-19). 2020 [internet publication]. [Full text](#)
849. Radia T, Williams N, Agrawal P, et al. Multi-system inflammatory syndrome in children & adolescents (MIS-C): a systematic review of clinical features and presentation. *Paediatr Respir Rev*. 2020 Aug 11 [Epub ahead of print]. [Full text](#) [Abstract](#)
850. Davies P, Evans C, Kanthimathinathan HK, et al. Intensive care admissions of children with paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS) in the UK: a multicentre observational study. *Lancet Child Adolesc Health*. 2020 Jul 9 [Epub ahead of print]. [Full text](#) [Abstract](#)
851. Harwood R, Allin B, Jones CE, et al. A national consensus management pathway for paediatric inflammatory multisystem syndrome temporally associated with COVID-19 (PIMS-TS): results of a national Delphi process. *Lancet Child Adolesc Health*. 2020 Sep 18 [Epub ahead of print]. [Full text](#) [Abstract](#)
852. Shulman ST. Pediatric coronavirus disease-2019-associated multisystem inflammatory syndrome. *J Pediatric Infect Dis Soc*. 2020 Jul 13;9(3):285-6. [Full text](#) [Abstract](#)
853. Carter MJ, Fish M, Jennings A, et al. Peripheral immunophenotypes in children with multisystem inflammatory syndrome associated with SARS-CoV-2 infection. *Nat Med*. 2020 Aug 18 [Epub ahead of print]. [Full text](#) [Abstract](#)
854. Sokolovsky S, Soni P, Hoffman T, et al. COVID-19 associated Kawasaki-like multisystem inflammatory disease in an adult. *Am J Emerg Med*. 2020 Jun 25 [Epub ahead of print]. [Full text](#) [Abstract](#)
855. Jones I, Bell LCK, Manson JJ, et al. An adult presentation consistent with PIMS-TS. *Lancet Rheumatol*. 2020 Jul 10 [Epub ahead of print]. [Full text](#) [Abstract](#)

856. Shaigany S, Gnirke M, Guttman A, et al. An adult with Kawasaki-like multisystem inflammatory syndrome associated with COVID-19. *Lancet*. 2020 Jul 10 [Epub ahead of print]. [Full text](#) [Abstract](#)
857. Dhir SK, Kumar J, Meena J, et al. Clinical features and outcome of SARS-CoV-2 infection in neonates: a systematic review. *J Trop Pediatr*. 2020 Aug 28 [Epub ahead of print]. [Full text](#) [Abstract](#)
858. Koehler P, Cornely OA, Böttiger BW, et al. COVID-19 associated pulmonary aspergillosis. *Mycoses*. 2020 Jun;63(6):528-34. [Full text](#) [Abstract](#)
859. Blaize M, Mayaux J, Nabet C, et al. Fatal invasive aspergillosis and coronavirus disease in an immunocompetent patient. *Emerg Infect Dis*. 2020 Apr 28;26(7). [Full text](#) [Abstract](#)
860. van Arkel ALE, Rijpstra TA, Belderbos HNA, et al. COVID-19 associated pulmonary aspergillosis. *Am J Respir Crit Care Med*. 2020 May 12 [Epub ahead of print]. [Full text](#) [Abstract](#)
861. Alanio A, Dellièrè S, Fodil S, et al. Prevalence of putative invasive pulmonary aspergillosis in critically ill patients with COVID-19. *Lancet Respir Med*. 2020 Jun;8(6):e48-9. [Full text](#) [Abstract](#)
862. Wang J, Yang Q, Zhang P, et al. Clinical characteristics of invasive pulmonary aspergillosis in patients with COVID-19 in Zhejiang, China: a retrospective case series. *Crit Care*. 2020 Jun 5;24(1):299. [Full text](#) [Abstract](#)
863. Verweij PE, Gangneux JP, Bassetti M, et al. Diagnosing COVID-19-associated pulmonary aspergillosis. *Lancet Microbe*. 2020 Jun;1(2):e53-5. [Full text](#) [Abstract](#)
864. Wang F, Wang H, Fan J, et al. Pancreatic injury patterns in patients with COVID-19 pneumonia. *Gastroenterology*. 2020 Apr 1;159(1):367-70. [Full text](#) [Abstract](#)
865. Bruno G, Fabrizio C, Santoro CR, et al. Pancreatic injury in the course of coronavirus disease 2019: a not-so-rare occurrence. *J Med Virol*. 2020 Jun 4 [Epub ahead of print]. [Full text](#) [Abstract](#)
866. McNabb-Baltar J, Jin DX, Grover AS, et al. Lipase elevation in patients with COVID-19. *Am J Gastroenterol*. 2020 Jun 3 [Epub ahead of print]. [Full text](#) [Abstract](#)
867. Gubatan J, Levitte S, Patel A, et al. Prevalence, risk factors and clinical outcomes of COVID-19 in patients with a history of pancreatitis in Northern California. *Gut*. 2020 Jun 3 [Epub ahead of print]. [Full text](#) [Abstract](#)
868. Lazarian G, Quinquenel A, Bellal M, et al. Autoimmune haemolytic anaemia associated with COVID-19 infection. *Br J Haematol*. 2020 Jul;190(1):29-31. [Full text](#) [Abstract](#)
869. Bomhof G, Mutsaers PGNJ, Leebeek FWG, et al. COVID-19-associated immune thrombocytopenia. *Br J Haematol*. 2020 Jul;190(2):e61-4. [Full text](#) [Abstract](#)
870. See Tsao H, Chason HM, Fearon DM, et al. Immune thrombocytopenia (ITP) in a SARS-CoV-2-positive pediatric patient. *Pediatrics*. 2020 May [Epub ahead of print]. [Full text](#) [Abstract](#)
871. Tang MW, Nur E, Biemond BJ. Immune thrombocytopenia due to COVID-19 during pregnancy. *Am J Hematol*. 2020 Aug;95(8):E191-2. [Full text](#) [Abstract](#)

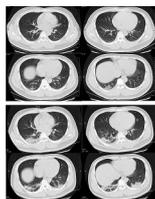
872. Muller I, Cannavaro D, Dazzi D, et al. SARS-CoV-2-related atypical thyroiditis. *Lancet Diabetes Endocrinol*. 2020 Jul 30 [Epub ahead of print]. [Full text](#) [Abstract](#)
873. Brancatella A, Ricci D, Viola N, et al. Subacute thyroiditis after SARS-CoV-2 infection. *J Clin Endocrinol Metab*. 2020 Jul 1;105(7):dgaa276. [Full text](#) [Abstract](#)
874. Centre for Evidence-Based Medicine; Greenhalgh T, Treadwell J, Burrow R, et al. NEWS (or NEWS2) score when assessing possible COVID-19 patients in primary care? 2020 [internet publication]. [Full text](#)
875. George PM, Barratt SL, Condliffe R, et al. Respiratory follow-up of patients with COVID-19 pneumonia. *Thorax*. 2020 Aug 24 [Epub ahead of print]. [Full text](#) [Abstract](#)
876. Centers for Disease Control and Prevention. Interim guidance for public health professionals managing people with COVID-19 in home care and isolation who have pets or other animals. 2020 [internet publication]. [Full text](#)
877. Centers for Disease Control and Prevention. Coronavirus disease 2019 (COVID-19): COVID-19 and animals. 2020 [internet publication]. [Full text](#)
878. Shi J, Wen Z, Zhong G, et al. Susceptibility of ferrets, cats, dogs, and other domesticated animals to SARS-coronavirus 2. *Science*. 2020 May 29;368(6494):1016-20. [Full text](#) [Abstract](#)
879. IDEXX Laboratories. Leading veterinary diagnostic company sees no COVID-19 cases in pets. 2020 [internet publication]. [Full text](#)
880. Newman A, Smith D, Ghai RR, et al. First reported cases of SARS-CoV-2 infection in companion animals: New York, March-April 2020. *MMWR Morb Mortal Wkly Rep*. 2020 Jun 12;69(23):710-3. [Full text](#) [Abstract](#)
881. Halfmann PJ, Hatta M, Chiba S, et al. Transmission of SARS-CoV-2 in domestic cats. *N Engl J Med*. 2020 Aug 6 [Epub ahead of print]. [Full text](#) [Abstract](#)
882. Centers for Disease Control and Prevention. Coronavirus disease 2019 (COVID-19): if you have pets. 2020 [internet publication]. [Full text](#)
883. Phelan D, Kim JH, Chung EH. A game plan for the resumption of sport and exercise after coronavirus disease 2019 (COVID-19) infection. *JAMA Cardiol*. 2020 May 13 [Epub ahead of print]. [Full text](#) [Abstract](#)
884. American Academy of Pediatrics. COVID-19 interim guidance: return to sports. 2020 [internet publication]. [Full text](#)

## Images



*Figure 1: Illustration revealing ultrastructural morphology exhibited by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) when viewed with electron microscopically*

*Centers for Disease Control and Prevention*



*Figure 2: Transverse CT scans from a 32-year-old man, showing ground-glass opacity and consolidation of lower lobe of right lung near the pleura on day 1 after symptom onset (top panel), and bilateral ground-glass opacity and consolidation on day 7 after symptom onset*

*Xu XW et al. BMJ. 2020;368:m606*

# Disclaimer

BMJ Best Practice is intended for licensed medical professionals. BMJ Publishing Group Ltd (BMJ) does not advocate or endorse the use of any drug or therapy contained within this publication nor does it diagnose patients. As a medical professional you retain full responsibility for the care and treatment of your patients and you should use your own clinical judgement and expertise when using this product.

This content is not intended to cover all possible diagnosis methods, treatments, follow up, drugs and any contraindications or side effects. In addition, since such standards and practices in medicine change as new data become available, you should consult a variety of sources. We strongly recommend that you independently verify specified diagnosis, treatments and follow-up and ensure it is appropriate for your patient within your region. In addition, with respect to prescription medication, you are advised to check the product information sheet accompanying each drug to verify conditions of use and identify any changes in dosage schedule or contraindications, particularly if the drug to be administered is new, infrequently used, or has a narrow therapeutic range. You must always check that drugs referenced are licensed for the specified use and at the specified doses in your region.

Information included in BMJ Best Practice is provided on an “as is” basis without any representations, conditions or warranties that it is accurate and up to date. BMJ and its licensors and licensees assume no responsibility for any aspect of treatment administered to any patients with the aid of this information. To the fullest extent permitted by law, BMJ and its licensors and licensees shall not incur any liability, including without limitation, liability for damages, arising from the content. All conditions, warranties and other terms which might otherwise be implied by the law including, without limitation, the warranties of satisfactory quality, fitness for a particular purpose, use of reasonable care and skill and non-infringement of proprietary rights are excluded.

Where BMJ Best Practice has been translated into a language other than English, BMJ does not warrant the accuracy and reliability of the translations or the content provided by third parties (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages). BMJ is not responsible for any errors and omissions arising from translation and adaptation or otherwise.

Where BMJ Best Practice lists drug names, it does so by recommended United States Adopted Names (USANs) only. It is possible that certain drug formularies might refer to the same drugs using different names.

Please note that recommended formulations and doses may differ between drug databases drug names and brands, drug formularies, or locations. A local drug formulary should always be consulted for full prescribing information.

Treatment recommendations in BMJ Best Practice are specific to patient groups. Care is advised when selecting the integrated drug formulary as some treatment recommendations are for adults only, and external links to a pediatric formulary do not necessarily advocate use in children (and vice-versa). Always check that you have selected the correct drug formulary for your patient.

Where your version of BMJ Best Practice does not integrate with a local drug formulary, you should consult a local pharmaceutical database for comprehensive drug information including contraindications, drug interactions, and alternative dosing before prescribing.

## Interpretation of numbers

Regardless of the language in which the content is displayed, numerals are displayed according to the original English-language numerical separator standard. For example 4 digit numbers shall not include a comma nor a decimal point; numbers of 5 or more digits shall include commas; and numbers stated to be less than 1 shall be depicted using decimal points. See Figure 1 below for an explanatory table.

BMJ accepts no responsibility for misinterpretation of numbers which comply with this stated numerical separator standard.

This approach is in line with the guidance of the [International Bureau of Weights and Measures Service](#).

## Figure 1 – BMJ Best Practice Numeral Style

5-digit numerals: 10,000

4-digit numerals: 1000

numerals < 1: 0.25

Our full website and application terms and conditions can be found here: [Website Terms and Conditions](#).

### Contact us

+ 44 (0) 207 111 1105

support@bmj.com

BMJ

BMA House

Tavistock Square

London

WC1H 9JR

UK

# BMJ Best Practice

# Contributors:

---

## // Authors:

---

### **Nicholas J. Beeching, MA, BM BCh, FRCP, FRACP, FFTM RCPS (Glasg), FESCMID, DCH, DTM&H**

Consultant and Honorary Senior Lecturer in Infectious Diseases

Royal Liverpool University Hospital and Liverpool School of Tropical Medicine, Liverpool, UK

DISCLOSURES: NJB is partially supported by the National Institute of Health Research Health Protection Unit (NIHR HPRU) in Emerging and Zoonotic Infections at University of Liverpool in partnership with Public Health England (PHE), in collaboration with Liverpool School of Tropical Medicine. He is affiliated with Liverpool School of Tropical Medicine. The views expressed are those of the author and not necessarily those of the NHS, the NIHR, the Department of Health, or PHE.

---

### **Tom E. Fletcher, MBE, PhD, MBChB, MRCP, DTM&H**

Senior Clinical Lecturer and Defence Consultant in Infectious Diseases

Royal Liverpool University Hospital and Liverpool School of Tropical Medicine, Liverpool, UK

DISCLOSURES: TEF is a consultant/expert panel member to the World Health Organization, and is funded by the UK Surgeon General, the NHS, and Liverpool School of Tropical Medicine. TEF is partially supported by the National Institute of Health Research Health Protection Unit (NIHR HPRU) in Emerging and Zoonotic Infections at University of Liverpool in partnership with Public Health England (PHE), in collaboration with Liverpool School of Tropical Medicine. He is affiliated with Liverpool School of Tropical Medicine. He has received research grants from the Wellcome Trust, Medical Research Council, and the UK Public Health Rapid Support Team (UK-PHRST). The views expressed are those of the author and not necessarily those of the NHS, the NIHR, the Department of Health, or PHE.

---

### **Robert Fowler, MDCM, MS (Epi), FRCP(C)**

H. Barrie Fairley Professor of Critical Care

University Health Network and Interdepartmental Division of Critical Care Medicine, Director, Clinical Epidemiology and Health Care Research, Institute of Health Policy, Management and Evaluation, Dalla Lana School of Public Health, University of Toronto, Chief, Tory Trauma Program, Sunnybrook Hospital, Toronto, Canada

DISCLOSURES: RF declares that he has no competing interests.

## // Peer Reviewers:

---

### **William A. Petri, Jr., MD, PhD**

Professor

Division of Infectious Diseases and International Health, University of Virginia, Charlottesville, VA

DISCLOSURES: WAP declares that he has no competing interests.

---

### **Xin Zhang, MD, PhD**

Attending Physician

The Fifth Medical Center of PLA General Hospital, Clinical Division and Research Center of Infectious Disease, Beijing, China

DISCLOSURES: XZ declares that he has no competing interests.

---

### **Ran Nir-Paz, MD**

Associate Professor in Medicine

Department of Clinical Microbiology and Infectious Diseases, Hadassah Hebrew University Medical Center, Jerusalem, Israel

DISCLOSURES: RNP has received research grants from US-Israel Binational Science Foundation, Hebrew University, Rosetrees Trust, and Speedx. He is chair of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) Study Group for Mycoplasma and Chlamydia Infections (ESGMAC). RNP is a consultant for and has stocks in eDAS Healthcare. He is also chairperson of the Israeli Society for Infectious Diseases guidelines committee.