BMJ Best Practice

# Coronavirus disease 2019 (COVID-19)

The right clinical information, right where it's needed

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# Summary


- The situation is evolving rapidly with global case counts and deaths increasing each day.
- The World Health Organization has declared the COVID-19 outbreak a pandemic and rates the global risk assessment as very high.
- Community transmission is occurring in many countries, but it is uncertain how easily the virus spreads between people. Clinical trials and investigations to learn more about the virus, its origin, and how it affects humans are ongoing.

# Definition

Coronavirus disease 2019 (COVID-19) is a potentially severe acute respiratory infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The virus was identified as the cause of an outbreak of pneumonia of unknown cause in Wuhan City, Hubei Province, China, in December 2019.[1] The clinical presentation is 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.

The International Committee on Taxonomy of Viruses has confirmed SARS-CoV-2 as the name of the virus owing to the virus's genetic similarity to the SARS-CoV virus, but taking into account that there may be differences in disease spectrum and transmission.[2] [3] The World Health Organization has confirmed COVID-19 (a shortened version of coronavirus disease 2019) as the name of the disease that SARS-CoV-2 infection causes.[4] Prior to this, the virus and/or disease was known by various names including novel coronavirus (2019-nCoV), 2019-nCoV, or variations on this.

# Epidemiology

The World Health Organization (WHO) was informed of 44 cases of pneumonia of unknown microbial aetiology associated with Wuhan City, Hubei Province, China on 31 December 2019. Most of the patients in the outbreak reported a link to a large seafood and live animal market (Huanan South China Seafood Market).[16] The WHO announced that a novel coronavirus had been detected in samples taken from these patients. Laboratory tests ruled out severe acute respiratory syndrome coronavirus (SARS-CoV), Middle East respiratory syndrome (MERS)-CoV, influenza, avian influenza, and other common respiratory pathogens.[17]

Since then, the outbreak has escalated rapidly, 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. The outbreak spread rapidly from a single city in China to the entire country in only 30 days.[15] The numbers of cases and deaths have surpassed the toll from the 2002-2003 outbreak of severe acute respiratory syndrome (SARS). The number of cases and deaths outside of China has overtaken the total number of cases and deaths in China.

Consult the resources below for updated information on case counts:

- [WHO: novel coronavirus (COVID-19) situation dashboard]
- [WHO: coronavirus disease (COVID-2019) situation reports]
- [CDC: coronavirus disease 2019 (COVID-19) in the US]
- [CDC: locations with confirmed COVID-19 cases, by WHO region]
- [National Health Committee of the People’s Republic of China: outbreak report]

The Chinese Center for Disease Control and Prevention recently published data from the largest case series to date (72,314 cases from 31 December 2019 to 11 February 2020). The majority of confirmed cases (87%) were aged 30 to 79 years, 1% were aged 9 years or younger, 1% were aged 10 to 19 years, and 3% were aged 80 years or older. Approximately 51% of patients were male and 49% were female. Nearly 4% of cases were in healthcare workers.[15]

In the US, older patients (aged ≥65 years) accounted for 31% of all cases, 45% of hospitalisations, 53% of intensive care unit admissions, and 80% of deaths, with the highest incidence of severe outcomes in patients aged ≥85 years.[19]

Infection in children is being reported much less commonly than among adults, and all cases so far have been in family clusters or in children who have a history of close contact with an infected patient.[11] [12] In a case series of 2143 paediatric patients in China, the median age of children was 7 years, and 56.6% of cases were in boys although this gender difference was not considered significant.[20]

# Aetiology

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.[1]

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 severe acute respiratory syndrome (SARS)-like coronaviruses from bats, but it is distinct from SARS-CoV and Middle East respiratory syndrome (MERS)-CoV.[21] [22] 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.[23]

[Fig-1]

Coronaviruses are a large family of enveloped RNA viruses, some of which cause illness in people (e.g., common cold, SARS, MERS), and others that circulate among mammals (e.g., bats, camels) and birds. Rarely, animal coronaviruses can spread to humans and subsequently spread between people, as was the case with SARS and MERS.

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.[6] [7] [24] While the potential animal reservoir and intermediary host(s) are unknown at this point, studies suggest they may derive from a recombinant virus between the bat coronavirus and an origin-unknown coronavirus; however, this is yet to be confirmed.[21] [22] [25] [26]

Transmission dynamics of the virus are currently unknown and the situation is evolving. Person-to-person spread has been confirmed in community and healthcare settings in China and other countries.[18] 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 Huanan South China Seafood Market, whereas only 8.6% of cases after this date were linked to the market. This confirms that person-to-person spread occurred among close contacts since the middle of December 2019, including infections in healthcare workers. One study of a family cluster of five patients in Shenzhen who had a history of travel to Wuhan City (with one other family member who did not travel to Wuhan City) found that person-to-person spread is possible in both hospital and family settings.[24] Nosocomial transmission in healthcare workers and patients has been reported in 41% of patients in one case series.[8] Transmission has been reported in long-term care facilities.[27]

 

It is uncertain how easily the virus spreads between people, but transmission in chains involving several links is increasingly recognised. Similar to SARS and MERS, it is thought that human transmission occurs via respiratory droplets produced when a person sneezes or coughs.[28] The contribution to transmission by the presence of the virus in other body fluids is unknown; however, the virus has been detected in blood, saliva, tears, and conjunctival secretions, and faecal transmission may also be possible.[29] [30] [31] [32]

There is mounting evidence that spread from asymptomatic carriers can occur and this has been observed in endemic areas.[33] [34] [35] [36] [37]

Anecdotal reports suggest that some people can act as superspreaders early in the course of their infection. These individuals can pass the infection on to large numbers of contacts, including healthcare workers. This phenomenon is well documented for infections such as SARS and Ebola virus infection, and more recently with MERS.[38] [39] Some of these individuals are also supershedders of virus, but the reasons underlying superspreader events are often more complex than just excess virus shedding and can include a variety of behavioural and environmental factors.[38]

It is unknown whether perinatal transmission or transmission via breastfeeding is possible; however perinatal transmission has been suspected in one case.[40] [41] Retrospective reviews of pregnant women with COVID-19 found that there is no evidence for intrauterine infection caused by vertical transmission in women who develop the infection late in pregnancy. However, there is currently a lack of data about the risk of transmission to the newborn during vaginal delivery.[42] [43] [44]

# Pathophysiology

Current estimates of the incubation period range from 1 to 14 days, according to the World Health Organization and the US Centers for Disease Control and Prevention.[45] [46] The median incubation period has been estimated to be approximately 5 days.[24] [47] Transmission may be possible during the incubation period.[48]

Preliminary reports suggest that the reproductive number ($R_0$), the number of people who acquire the infection from an infected person, is approximately 2.2.[24] [49] However, as the situation is still evolving, the $R_0$ may actually be higher or lower. The secondary attack rate for SARS-CoV-2 is estimated to be 0.45% for close contacts of US patients.[50]

While the pathophysiology of this condition is currently unknown, it is thought that the virus binds to the angiotensin-converting enzyme-2 (ACE2) receptor in humans, which suggests that it may have a similar pathogenesis to SARS.[22] [51] However, 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 to SARS-CoV.[52] A furin-like cleavage site has been identified in the spike protein of the virus; this does not exist in other SARS-like coronaviruses.[53]

Based on an analysis of single-cell RNA sequencing datasets derived from major human physiological systems, the organs considered more vulnerable to SARS-CoV-2 infection due to their ACE2 expression levels include the lungs, heart, oesophagus, kidneys, bladder, and ileum.[54]

High viral loads have been detected in nasal and throat swabs soon after symptom onset, and it is thought that the viral shedding pattern may be similar to that of patients with influenza. An asymptomatic patient

was found to have a similar viral load compared with symptomatic patients.[55] The median duration of viral shedding is approximately 20 days in survivors.[56]

# Classification

## World Health Organization: clinical classification of COVID-19[5]

Mild illness

- Patients with uncomplicated upper respiratory tract viral infection may have non-specific symptoms such as fever, fatigue, cough (with or without sputum production), anorexia, malaise, muscle pain, sore throat, dyspnoea, nasal congestion, or headache. Rarely, patients may also present with diarrhoea, nausea, and vomiting.
- Older and/or immunosuppressed patients may present with atypical symptoms.
- Symptoms due to physiological adaptations of pregnancy or adverse pregnancy events (e.g., dyspnoea, fever, gastrointestinal symptoms, fatigue) may overlap with COVID-19 symptoms.

Pneumonia

- Adults: pneumonia with no signs of severe pneumonia (see below) and no need for supplemental oxygen.
- Children: pneumonia with cough or difficulty breathing plus fast breathing (i.e., <2 months of age: ≥60 breaths/minute; 2-11 months of age: ≥50 breaths/minute; 1-5 years years of age: ≥40 breaths/minute) and no signs of severe pneumonia (see below).

Severe pneumonia in adults and adolescents

- Fever or suspected respiratory infection plus one of the following:
    - Respiratory rate >30 breaths/minute
    - Severe respiratory distress
    - $SpO_2$ ≤93% on room air.

Severe pneumonia in children

- Cough or difficulty breathing plus at least one of the following:
    - Central cyanosis or $SpO_2$ <90%
    - Severe respiratory distress (e.g., grunting, very severe chest indrawing)
    - Signs of pneumonia with a general danger sign (i.e., inability to breastfeed or drink, lethargy or unconsciousness, or convulsions).
- Other signs of pneumonia may be present in children including chest indrawing or fast breathing (i.e., <2 months of age: ≥60 breaths/minute; 2-11 months of age: ≥50 breaths/minute; 1-5 years years of age: ≥40 breaths/minute).
- While the diagnosis is made on clinical grounds, chest imaging may identify or exclude some pulmonary complications.

 

# Primary prevention

General prevention measures

- The only way to prevent infection is to avoid exposure to the virus and people should be advised to:[59] [60]
    - Wash hands often with soap and water or an alcohol-based hand sanitiser and avoid touching the eyes, nose, and mouth with unwashed hands
    - Avoid close contact with people (i.e., maintain a distance of at least 1 metre [3 feet]), particularly those who have a fever or are coughing or sneezing
    - 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 with their healthcare provider
    - Avoid direct unprotected contact with live animals and surfaces in contact with live animals when visiting live markets in affected areas
    - Avoid the consumption of raw or undercooked animal products, and handle raw meat, milk, or animal organs with care as per usual good food safety practices.
- [WHO: coronavirus disease (COVID-19) advice for the public]

Medical masks

- The World Health Organization (WHO) does not recommend that people wear a medical mask in community settings if they do not have respiratory symptoms as there is no evidence available on its usefulness to protect people who are not ill. However, masks may be worn in some countries according to local cultural habits. Individuals with fever and/or respiratory symptoms are advised to wear a mask, particularly in endemic areas.[61]
- It is mandatory to wear a medical mask in public in certain areas of China, and local guidance should be consulted for more information.
- It is important to wash your hands with soap and water (or an alcohol-based sanitiser) prior to putting on a face mask.[62]
- [BMJ: facemasks for the prevention of infection in healthcare and community settings]

Screening and quarantine

- People travelling 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 modelled to miss up to 50% of cases of COVID-19, particularly those with no symptoms during an incubation period, which may exceed 10 days.[63] 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.[64]
- Enforced quarantine has been used in some countries to isolate easily identifiable cohorts of people at potential risk of recent exposure (e.g., groups evacuated by aeroplane from affected areas, or groups on cruise ships with infected people on board).[65] The psychosocial effects of enforced quarantine may have long-lasting repercussions.[66] [67]

Vaccine

- There is currently no vaccine available. Vaccines are in development, but it may take some time before a vaccine is available.[68] [69] An mRNA vaccine (mRNA-1273) has been shipped to the National Institute of Allergy and Infectious Diseases for phase 1 clinical trials in the US.[70] The vaccine includes a short segment of genetic code copied from the virus. The trial started in humans on 16 March 2020. Clinical trials in humans have also started on an experimental adenoviral vector vaccine in China.[71]

# Screening

## Management of contacts

People who may have been exposed to individuals with suspected COVID-19 (including healthcare workers) should be advised to monitor their health for 14 days from the last day of possible contact, and seek immediate medical attention if they develop any symptoms, particularly fever, respiratory symptoms such as coughing or shortness of breath, or diarrhoea.[106] Some people may be put into voluntary or compulsory quarantine depending on the guidance from local health authorities.

## Screening of travellers

Exit and entry screening may be recommended in some countries, particularly when repatriating nationals from affected areas. Travellers returning from affected areas should self-monitor for symptoms for 14 days and follow local protocols of the receiving country. Some countries may require returning travellers to enter quarantine. Travellers who develop symptoms are advised to contact their local health care provider, preferably by phone.[107]

# Secondary prevention

Early recognition of new cases is the cornerstone of prevention of transmission. Immediately isolate all suspected and confirmed cases and implement recommended infection prevention and control procedures according to local protocols, including standard precautions at all times, and contact, droplet, and airborne precautions while the patient is symptomatic.[73] COVID-19 is a notifiable disease; report all suspected and confirmed cases to your local health authorities.

Detailed guidance on infection prevention and control measures are available from the World Health Organization and the Centers for Disease Control and Prevention:

- [WHO: infection prevention and control during health care when novel coronavirus (nCoV) infection is suspected]
- [CDC: interim infection prevention and control recommendations for patients with confirmed coronavirus disease 2019 (COVID-19) or persons under investigation for COVID-19 in healthcare settings]



 

# Case history

## Case history #1

A 61-year-old man presents to hospital on 3 March 2020 with fever, cough, and difficulty breathing. He also reports feeling very tired and unwell. He has a history of congestive heart failure, which is controlled with medication. On examination, his pulse is 120 bpm and his temperature is 38.7°C (101.6°F). Chest x-ray shows bilateral lung infiltrates. He is admitted to hospital in an isolation room and is started on oxygen, intravenous fluids, empirical antibiotics, and paracetamol. Later that day, he tests positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on real-time reverse transcriptase polymerase chain reaction testing. The patient develops respiratory distress 7 days after admission and is started on mechanical ventilation.

## Case history #2

A 30-year-old man presents to his general practitioner on 14 January 2020 with a bad cough. He has had the cough for 4 days and now feels a little short of breath. He also has a headache and reports that his muscles ache. On examimation, his pulse is 100 bpm and his temperature is 38.5°C (101.3°F). The patient reports that he returned from a business trip in mainland China 6 days ago.

## Other presentations

Other non-specific mild symptoms may include anorexia, confusion, dizziness, sore throat, rhinorrhoea, and sputum production. Some patients may present with chest pain or haemoptysis. Gastrointestinal symptoms such as diarrhoea, nausea, vomiting, and abdominal pain have been reported rarely, although this may be underestimated.[6] [7] [8] [9] [10] Some patients may be minimally symptomatic or asymptomatic, especially children.[11] [12] [13] [14]

Approximately 80% of patients present with mild illness, 14% present with severe illness, and 5% present with critical illness.[15] Patients with severe illness may have signs and symptoms of viral pneumonia, or complications including acute distress syndrome, acute cardiac injury, arrhythmias, acute kidney injury, secondary infection, sepsis, or shock.[6] [7] [8]

Atypical presentations may occur, especially in older patients or patients who are immunosuppressed, as the full spectrum of clinical illness is yet to be characterised.



# 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 and who report a travel history to an affected area or close contact with a suspected or confirmed case in the 14 days prior to symptom onset. Evaluation should be performed according to pneumonia severity indexes and sepsis guidelines (if sepsis is suspected) in all patients with severe illness.

It is important that general practitioners avoid in-person assessment of patients with suspected COVID-19 in primary care when possible.[72] Algorithms for dealing with these patients are available:

- [BMJ: covid-19 in primary care (UK)]

There is limited information available to characterise the spectrum of clinical illness. Much of the information in this section is based on early evidence, analysis of case series and reports (mostly limited to hospitalised patients with pneumonia), and data from previous betacoronavirus infections such as severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). Consult local guidance for further detailed information as the situation is evolving rapidly.

## Infection prevention and control

Triage all patients on admission and immediately isolate all suspected and confirmed cases in an area separate from other patients. Suspected patients should be given a mask and kept at least 1 metre (3 feet) from other suspected patients. Implement appropriate infection prevention and control procedures. Screening questionnaires may be helpful. COVID-19 is a notifiable disease; report all suspected and confirmed cases to your local health authorities.

The World Health Organization (WHO) recommends the following basic principles:[73]

- Immediately isolate all suspected cases in an area that is separate from other patients
- Implement standard precautions at all times:
    - Practice hand and respiratory hygiene
    - Offer a medical mask to patients who can tolerate one
    - Wear personal protective equipment
    - Prevent needlestick and sharps injury
    - Practice safe waste management, environmental cleaning, and sterilisation of patient care equipment and linen
- Implement additional contact and droplet precautions until the patient is asymptomatic:
    - Place patients in adequately ventilated single rooms; when single rooms are not available, place all suspected cases together in the same ward
    - 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
    - Consider limiting the number of healthcare workers, family members, and visitors in contact with the patient, ensuring optimal patient care and psychosocial support for the patient
    - Consider placing patients in negative pressure rooms, if available
- Implement airborne precautions when performing aerosol-generating procedures
- All specimens collected for laboratory investigations should be regarded as potentially infectious.



 

It is important to disinfect inanimate surfaces in the surgery or hospital as patients may touch and contaminate surfaces such as door handles and desktops.[74] The median half-life of the virus is approximately 1 hour as an aerosol, 4 hours on copper, 24 hours on cardboard, and 72 hours on stainless steel and plastic, based on initial data.[75]

Detailed guidance on infection prevention and control procedures are available from the WHO and the Centers for Disease Control and Prevention (CDC):

- [WHO: infection prevention and control during health care when novel coronavirus (nCoV) infection is suspected]
- [CDC: interim infection prevention and control recommendations for patients with suspected or confirmed coronavirus disease 2019 (COVID-19) in healthcare settings]

## History

Take a detailed history to ascertain the level of risk for COVID-19 and assess the possibility of other causes. Travel history may be key; it is crucial for timely diagnosis and to prevent further transmission.

The diagnosis should be suspected in patients with fever and/or signs/symptoms of acute respiratory illness (e.g., cough, dyspnoea) who reside in or have travelled to a country/area or territory reporting local transmission of COVID-19 or who report close contact with a confirmed or probable case of COVID-19 in the 14 days prior to symptom onset.[76] [77]

## Clinical presentation

The clinical presentation resembles viral pneumonia, and the severity of illness ranges from mild to severe. Approximately 80% of patients present with mild illness, 14% present with severe illness, and 5% present with critical illness.[15]

Illness severity is associated with older age and the presence of underlying health conditions.[15] Older patients and/or those with comorbidities may present with mild symptoms, but have a high risk of deterioration.[5] The most prevalent comorbidities in patients with COVID-19 are hypertension, diabetes, cardiovascular disease, and respiratory disease.[78]

The most common symptoms are:[6] [7] [8] [9] [79] [80]

- Fever
- Cough
- Dyspnoea
- Myalgia
- Fatigue.

Less common symptoms include:

- Anorexia
- Sputum production
- Sore throat

- Confusion
- Dizziness
- Headache
- Rhinorrhoea
- Chest pain
- Haemoptysis
- Diarrhoea
- Nausea/vomiting
- Abdominal pain
- Conjunctival congestion.

Some patients may be minimally symptomatic or asymptomatic. Mild illness is defined as patients with an uncomplicated upper respiratory tract infection with non-specific symptoms such as fever, cough (with or without sputum production), fatigue, anorexia, malaise, myalgia, sore throat, dyspnoea, nasal congestion, or headache. Rarely patients may have gastrointestinal symptoms. The most common diagnosis in patients with severe COVID-19 is severe pneumonia.[5]

Approximately 90% of patients present with more than one symptom, and 15% of patients present with fever, cough, and dyspnoea.[7] It appears that fewer patients have prominent upper respiratory tract or gastrointestinal symptoms compared with SARS, MERS, or influenza.[6] [7] Patients may present with nausea or diarrhoea 1 to 2 days prior to onset of fever and breathing difficulties.[8]

A retrospective case series of 62 patients in Zhejiang province found that the clinical features were less severe than those of the primary infected patients from Wuhan City, indicating that second-generation infection may result in milder infection. This phenomenon was also reported with MERS.[81]

Children

- Children are typically asymptomatic or present with mild symptoms (e.g., brief and rapidly resolving fever, mild cough, sore throat, congestion, rhinorrhoea).[11] [12] [13] [14] [82] In a case series of 2143 paediatric patients in China, over 90% of children were asymptomatic or had a mild or moderate illness; 16% were asymptomatic and had no radiological evidence of pneumonia.[20] However, it is important to note that children may have signs of pneumonia on chest imaging despite having minimal or no symptoms.[83]
- There is one case report of an infant who had mainly gastrointestinal symptoms.[84]
- Moderate to severe illness has been reported in children.[85]
- Co-infections may be more common in children.[83]

Pregnant women

- Retrospective reviews of pregnant women with COVID-19 found that the clinical characteristics in pregnant women were similar to those reported for non-pregnant adults.[43]
- It is important to note that symptoms such as fever, dyspnoea, and fatigue may overlap with symptoms due to physiological adaptations of pregnancy or adverse pregnancy events.[5]



 

Perform a physical examination. 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, tachypnoea, or cyanosis accompanying hypoxia.

## Initial investigations

Order the following investigations in all patients with severe illness:

- Pulse oximetry
- ABG (as indicated to detect hypercarbia or acidosis)
- FBC
- Comprehensive metabolic panel
- Coagulation screen
- Inflammatory markers (serum procalcitonin and C-reactive protein)
- Serum troponin
- Serum lactate dehydrogenase
- Serum creatine kinase.

The most common laboratory abnormalities in patients hospitalised with pneumonia include leukopenia, lymphopenia, leukocytosis, elevated liver transaminases, elevated lactate dehydrogenase, and elevated C-reactive protein. Other abnormalities include neutrophilia, thrombocytopenia, decreased haemoglobin, decreased albumin, and renal impairment.[6] [7] [8] [80] [86]

Pulse oximetry may reveal low oxygen saturation ($SpO_2$ <90%).

**[VIDEO: Radial artery puncture animated demonstration ]**

## Blood and sputum cultures

Collect blood and sputum specimens for culture in all patients to rule out other causes of lower respiratory tract infection and sepsis, especially patients with an atypical epidemiological history. Specimens should be collected prior to starting empirical antimicrobials if possible.[5]

## Molecular testing

Molecular testing is required to confirm the diagnosis. Diagnostic tests should be performed according to guidance issued by local health authorities and should adhere to appropriate biosafety practices. If testing is not available nationally, specimens should be shipped to an appropriate reference laboratory. Specimens for testing should be collected under appropriate infection prevention and control procedures.

The CDC recommends that the following people are prioritised for testing:[87]

- Hospitalised patients with signs and symptoms of COVID-19
- Other symptomatic people aged 65 years and older and/or those with a chronic medical condition or who are immunocompromised

- Symptomatic people who have had close contact with a suspected or confirmed case, or have a history of travel from an affected geographical area, within 14 days of symptom onset.

Symptomatic pregnant women should also be prioritised in order to enable access to specialised care.[5]

Perform a nucleic acid amplification test, such as real-time reverse-transcription polymerase chain reaction (RT-PCR), for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in all patients with suspected infection, with confirmation by nucleic acid sequencing when necessary.[88]

- Collect upper respiratory specimens (nasopharyngeal and oropharyngeal swab or wash) in ambulatory patients and/or lower respiratory specimens (sputum and/or endotracheal aspirate or bronchoalveolar lavage) in patients with more severe respiratory disease.
- Also consider collecting additional clinical specimens (e.g., blood, stool, urine).

One or more negative results do not rule out the possibility of infection. If a negative result is obtained from a patient with a high index of suspicion for COVID-19, additional specimens should be collected and tested, especially if only upper respiratory tract specimens were collected initially.[88] Guidelines recommend that two consecutive negative tests (at least one day apart) are required to exclude COVID-19; however, there is a case report of a patient who returned two consecutive negative results and didn't test positive until 11 days after symptom onset and confirmation of typical chest computed tomography (CT) findings.[89]

Collect nasopharyngeal swabs for testing to rule out infection with other respiratory pathogens (e.g., influenza, atypical pathogens) according to local guidance. It is important to note that co-infections can occur, and a positive test for a non-COVID-19 pathogen does not rule out COVID-19.[5] [90]

Serological testing is not available as yet, but assays are in development.[91] Serum samples can be stored to retrospectively define cases when validated serology tests become available.

## Imaging

All imaging procedures should be performed according to local infection prevention and control procedures to prevent transmission.

Chest x-ray

- 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.[6] [7] [92]

CT chest

- Consider ordering a CT scan of the chest. Abnormal chest CT findings have been reported in up to 97% of patients in one meta-analysis of 50,466 hospitalised patients.[79] CT is the primary imaging modality in China.[93]
- CT imaging generally shows bilateral multiple lobular and subsegmental areas of ground-glass opacity or consolidation in most patients, usually with a peripheral or posterior distribution, mainly in the lower lobes and less frequently in the right lower lobe. Consolidative opacities superimposed on ground-glass opacity may be found in a smaller number of cases, usually older patients. Other atypical features include interlobular or septal thickening (smooth or irregular), thickening of the adjacent pleura, subpleural involvement, crazy paving pattern, and air bronchograms. Some patients may rarely present with pleural effusion, pericardial effusion, bronchiectasis, cavitation, pneumothorax, lymphadenopathy, and round cystic changes. Atypical features appear to be more



 

common in the later stages of disease, or on disease progression. None of these findings appear to be specific or diagnostic for COVID-19.[6] [81] [94] Abnormalities can rapidly evolve from focal unilateral to diffuse bilateral ground-glass opacities that progress to, or co-exist with, consolidations within 1 to 3 weeks.[95] The greatest severity of CT findings is usually visible around day 10 after symptom onset, and imaging signs associated with clinical improvement (e.g., resolution of consolidative opacities, reduction in number of lesions and involved lobes) usually occur after week 2 of the disease.[94] 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.[96]

- Small nodular ground-glass opacities are the most common finding in children.[97] Consolidation with surrounding halo signs is a typical finding in children.[83]
- Evidence of viral pneumonia on CT may precede a positive RT-PCR result for SARS-CoV-2 in some patients.[91] However, CT imaging abnormalities may be present in minimally symptomatic or asymptomatic patients.[36] [95] Some patients may present with a normal chest finding despite a positive RT-PCR.[98]
- 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.[99]

# Risk factors

## Strong

### residence in/travel to affected area 14 days prior to symptom onset

- Diagnosis should be suspected in patients with fever and/or signs/symptoms of lower respiratory illness (e.g., cough, dyspnoea) who reside in, or have travelled to a country/area or territory reporting local transmission of COVID-19 in the 14 days prior to symptom onset.[57] [58]
- [WHO: novel coronavirus (COVID-19) situation dashboard]
- [CDC: locations with confirmed 2019-nCoV cases]

### close contact with infected individual

- Diagnosis should be suspected in patients with fever and/or signs/symptoms of lower respiratory illness (e.g., cough, dyspnoea) who report close contact with a confirmed or probable case of COVID-19 in the 14 days prior to symptom onset.[57] [58]

# History & examination factors

## Key diagnostic factors

### fever (common)

- Reported in 83% to 98% of patients in case series.[6] [7] [8] [79] [80] [100] In one case series, 44% of patients had a fever on presentation, but it developed in 89% of patients after hospitalisation.[9]

- Less common in children.[14]
- Children may not present with fever, or may have a brief and rapidly resolving fever.[11] [82]
- Patients may present with chills/rigors.
- The course of fever is not fully understood yet, but it may be prolonged and intermittent.

### cough (common)

- Reported in 57% to 82% of patients in case series.[6] [7] [8] [9] [79] [80] [100]
- Less common in children.[14]
- Cough is usually dry.

### dyspnoea (common)

- Reported in 18% to 55% of patients in case series.[6] [7] [8] [9] [80] [100]
- Median time from onset of symptoms to development of dyspnoea is 5 to 8 days.[6] [7] [8]

## Other diagnostic factors

### fatigue (common)

- Reported in 29% to 69% of patients in case series.[6] [8] [9] [80] [100]
- Patients may also report malaise.

### myalgia (common)

- Reported in 11% to 44% of patients in case series.[6] [7] [8] [9] [79] [100]

### anorexia (common)

- Reported in 40% of patients in case series.[8]

### sputum production/expectoration (common)

- Reported in 26% to 33% of patients in case series.[6] [8] [9] [100]

### sore throat (common)

- Reported in 5% to 17% of patients in case series, and usually presents early in the clinical course.[7] [8] [9] [100]
- Children may have pharyngeal erythema.[14]

### confusion (uncommon)

- Reported in 9% of patients in case series.[7]

### dizziness (uncommon)

- Reported in 9% to 12% of patients in case series.[8] [80]

### headache (uncommon)

- Reported in 6% to 14% of patients in case series.[6] [7] [8] [9] [80] [100]

### haemoptysis (uncommon)

- Reported in 1% to 5% of patients in case series.[6] [9]

### rhinorrhoea (uncommon)

- Reported in 4% to 5% of patients in case series.[7] [9]



 

### chest pain (uncommon)

- Reported in 2% to 5% of patients in case series.[6] [7]
- May indicate pneumonia.

### gastrointestinal symptoms (uncommon)

- Nausea, vomiting, and diarrhoea have been reported in 1% to 10% of patients in case series, although this may be underestimated.[6] [7] [8] [9] [80] [100] One case series reported gastrointestinal symptoms in nearly 40% of patients.[10]
- Abdominal pain has been reported in 2% of patients in case series.[8]
- Patients may present with nausea or diarrhoea 1 to 2 days prior to onset of fever and breathing difficulties.[8]

### conjunctival congestion (uncommon)

- Reported in <1% of patients in case series.[9]

### bronchial breath sounds (uncommon)

- May indicate pneumonia.

### tachypnoea (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 |
|---|---|
| **pulse oximetry**<br>• Order in patients with severe illness.<br>• Recommended in patients with respiratory distress and cyanosis. | **may show low oxygen saturation ($SpO_2$ <90%)** |
| **ABG**<br>• Order in patients with severe illness as indicated to detect hypercarbia or acidosis.<br>• Recommended in patients with respiratory distress and cyanosis who have low oxygen saturation ($SpO_2$ <90%). | **may show low partial oxygen pressure** |
| **FBC**<br>• Order in patients with severe illness.<br>• The most common laboratory abnormalities in patients hospitalised with pneumonia include leukopenia, lymphopenia, and leukocytosis. Other abnormalities include neutrophilia, thrombocytopenia, and decreased haemoglobin.[6] [7] [8] [86]<br>• Thrombocytopenia has been associated with increased risk of severe disease and mortality and may be useful as a clinical indicator for monitoring disease progression.[101] | **leukopenia; lymphopenia; leukocytosis** |
| **coagulation screen**<br>• Order in patients with severe illness.<br>• The most common abnormalities are elevated D-dimer and prolonged prothrombin time.[6] [7] [8]<br>• Non-survivors had significantly higher D-dimer levels and longer prothrombin time and activated partial thromboplastin time compared with survivors in one study.[102] | **elevated D-dimer; prolonged prothrombin time** |
| **comprehensive metabolic panel**<br>• Order in patients with severe illness.<br>• The most common laboratory abnormalities in patients hospitalised with pneumonia include elevated liver transaminases. Other abnormalities include decreased albumin and renal impairment.[6] [7]<br>• Liver function abnormalities may be more common in patients with COVID-19 compared with other types of pneumonia.[96] | **elevated liver transaminases; decreased albumin; renal impairment** |
| **serum procalcitonin**<br>• Order in patients with severe illness.<br>• May be elevated in patients with secondary bacterial infection.[6] [7] May be more common in children.[83] | **may be elevated** |
| **serum C-reactive protein**<br>• Order in patients with severe illness.<br>• May be elevated in patients with secondary bacterial infection.[6] [7] | **may be elevated** |
| **serum lactate dehydrogenase**<br>• Order in patients with severe illness.<br>• Elevated lactate dehydrogenase has been reported in 73% to 76% of patients.[6] [7] May be more common in patients with COVID-19 compared with other types of pneumonia.[96]<br>• Indicates liver injury or lysis of blood erythrocytes. | **may be elevated** |

| Test | Result |
|---|---|
| **serum creatine kinase**<br>• Order in patients with severe illness.<br>• Elevated creatine kinase has been reported in 13% to 33% of patients.[6] [7]<br>• Indicates muscle or myocardium injury. | **may be elevated** |
| **serum troponin level**<br>• Order in patients with severe illness.<br>• May be elevated in patients with cardiac injury.[6] | **may be elevated** |
| **blood and sputum cultures**<br>• Collect blood and sputum specimens for culture in all patients to rule out other causes of lower respiratory tract infection and sepsis, especially patients with an atypical epidemiological history.[5]<br>• Specimens should be collected prior to starting empirical antimicrobials if possible. | **negative for bacterial infection** |
| **real-time reverse transcription polymerase chain reaction (RT-PCR)**<br>• Molecular testing is required to confirm the diagnosis. Nucleic acid sequencing may be required to confirm the diagnosis.[88]<br>• Collect upper respiratory specimens (nasopharyngeal and oropharyngeal swab or wash) in ambulatory patients and/or lower respiratory specimens (sputum and/or endotracheal aspirate or bronchoalveolar lavage) in patients with more severe respiratory disease. Also consider collecting additional clinical specimens (e.g., blood, stool, urine). Specimens should be collected under appropriate infection prevention and control procedures.[88]<br>• If a negative result is obtained from a patient with a high index of suspicion for COVID-19, additional specimens should be collected and tested, especially if only upper respiratory tract specimens were collected initially.[88]<br>• Many tests are available under the US Food and Drug Administration's emergency-use authorisation scheme.[103] Tests are available in many laboratories worldwide and testing should be done according to instructions from local health authorities and adhere to appropriate biosafety practices. If testing is not available nationally, specimens should be shipped to an appropriate reference laboratory.<br>• Collect nasopharyngeal swabs to rule out influenza and other respiratory infections according to local guidance. It is important to note that co-infections can occur, and a positive test for a non-COVID-19 pathogen does not rule out COVID-19.[5] [90] | **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** |
| **chest x-ray**<br>• Order in all patients with suspected pneumonia.<br>• Unilateral lung infiltrates are found in 25% of patients, and bilateral lung infiltrates are found in 75% of patients.[6] [7] [92] | **unilateral or bilateral lung infiltrates** |
| **computed tomography (CT) chest**<br>• Consider a CT scan of the chest. Abnormal chest CT findings have been reported in up to 97% of patients in one meta-analysis of 50,466 hospitalised patients.[79] CT is the primary imaging modality in China.[93]<br>• CT imaging generally shows bilateral multiple lobular and subsegmental areas of ground-glass opacity or consolidation in | **bilateral ground-glass opacity or consolidation** |

| Test | Result |
| --- | --- |
| most patients, usually with a peripheral or posterior distribution, mainly in the lower lobes and less frequently in the right lower lobe. Consolidative opacities superimposed on ground-glass opacity may be found in a smaller number of cases, usually older patients. Other atypical features include interlobular or septal thickening (smooth or irregular), thickening of the adjacent pleura, subpleural involvement, crazy paving pattern, and air bronchograms. Some patients may rarely present with pleural effusion, pericardial effusion, bronchiectasis, cavitation, pneumothorax, lymphadenopathy, and round cystic changes. Atypical features appear to be more common in the later stages of disease, or on disease progression. None of these findings appear to be specific or diagnostic for COVID-19.[6] [81] [94] Abnormalities can rapidly evolve from focal unilateral to diffuse bilateral ground-glass opacities that progress to, or co-exist with, consolidations within 1 to 3 weeks.[95] The greatest severity of CT findings is usually visible around day 10 after symptom onset, and imaging signs associated with clinical improvement (e.g., resolution of consolidative opacities, reduction in number of lesions and involved lobes) usually occur after week 2 of the disease.[94] 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.[96]<br>• Small nodular ground-glass opacities are the most common finding in children.[97] Consolidation with surrounding halo signs is a typical finding in children.[83]<br>• Evidence of viral pneumonia on CT may precede a positive RT-PCR result for SARS-CoV-2 in some patients.[91] However, CT imaging abnormalities may be present in minimally symptomatic or asymptomatic patients.[36] [95]<br>• 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.[99]<br>[Fig-2] | |

## Emerging tests

| Test | Result |
| --- | --- |
| **serology**<br>• Serological testing is not available as yet, but assays are in development.[91] Serum samples can be stored to retrospectively define cases when validated serology tests become available. | **positive for SARS-CoV-2 virus antibodies** |



 

# Differential diagnosis

| Condition | Differentiating signs / symptoms | Differentiating tests |
|---|---|---|
| **Middle East respiratory syndrome (MERS)** | • Lack of travel history to mainland China or other affected areas, or of close contact with an infected person in the 14 days prior to symptom onset.<br>• Initial reports suggest that the clinical course of COVID-19 is less severe and the case fatality rate is lower compared with MERS (approximately 2% to 3% for COVID-19 versus 37% for MERS); however, there are no data to confirm this and the situation is rapidly evolving.[104]<br>• Gastrointestinal symptoms and upper respiratory tract symptoms appear to be less common in COVID-19 based on early data.[104] [105] | • Reverse-transcriptase polymerase chain reaction (RT-PCR): positive for MERS-CoV viral RNA. |
| **Severe acute respiratory syndrome (SARS)** | • There have been no cases of SARS reported since 2004.<br>• Lack of travel history to mainland China or other affected areas, or of close contact with an infected person in the 14 days prior to symptom onset.<br>• Initial reports suggest that the clinical course of COVID-19 is less severe and the case fatality rate is lower compared with SARS (approximately 2% to 3% for COVID-19 versus 10% for SARS); however, there are no data to confirm this and the situation is rapidly evolving.[104]<br>• Gastrointestinal symptoms and upper respiratory tract symptoms appear to be less common in COVID-19 based on early data.[104] [105] | • RT-PCR: positive for SARS-CoV viral RNA. |
| **Community-acquired pneumonia** | • Lack of travel history to mainland China or other affected areas, or of close contact with an infected | • Blood or sputum culture or molecular testing: positive for causative organism. |

| Condition | Differentiating signs / symptoms | Differentiating tests |
|---|---|---|
| | person in the 14 days prior to symptom onset.<br>• Differentiating COVID-19 from community-acquired respiratory tract infections is not possible from signs and symptoms. | |
| **Influenza infection** | • Lack of travel history to mainland China or other affected areas, or of close contact with an infected person in the 14 days prior to symptom onset.<br>• Differentiating COVID-19 from community-acquired respiratory tract infections is not possible from signs and symptoms. However, early reports suggest that sore throat is less common in COVID-19.[105] | • RT-PCR: positive for influenza A or B viral RNA. |
| **Common cold** | • Lack of travel history to mainland China or other affected areas, or of close contact with an infected person in the 14 days prior to symptom onset.<br>• Differentiating COVID-19 from community-acquired respiratory tract infections is not possible from signs and symptoms. However, early reports suggest that coryza and sore throat are less common in COVID-19.[105] | • RT-PCR: positive for causative organism, or negative for SARS-CoV-2 viral RNA. |
| **Avian influenza A (H7N9) virus infection** | • May be difficult to differentiate based on epidemiological history as avian influenza H7N9 is endemic in China.<br>• 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.<br>• Early reports suggest that sore throat is less common in COVID-19.[105] | • RT-PCR: positive for H7-specific viral RNA. |
| **Avian influenza A (H5N1) virus infection** | • Lack of travel history to mainland China or other affected areas, or of close | • RT-PCR: positive for H5N1 viral RNA. |



 

| Condition | Differentiating signs / symptoms | Differentiating tests |
|---|---|---|
| | contact with an infected person in the 14 days prior to symptom onset.<br>• 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.<br>• Early reports suggest that sore throat is less common in COVID-19.[105] | |
| **Other viral or bacterial respiratory infections** | • Lack of travel history to mainland China or other affected areas, or of close contact with an infected person in the 14 days prior to symptom onset.<br>• Differentiating COVID-19 from community-acquired respiratory tract infections is not possible from signs and symptoms.<br>• Adenovirus and *Mycoplasma* should be considered in clusters of pneumonia patients, especially in closed settings such as military camps and schools. | • Blood or sputum culture of molecular testing: positive for causative organism. |
| **Pulmonary tuberculosis** | • Consider diagnosis in endemic areas, especially in patients who are immunocompromised.<br>• History of symptoms is usually longer.<br>• Presence of night sweats and weight loss may help to differentiate. | • Chest x-ray: fibronodular opacities in upper lobes with or without cavitation; atypical pattern includes opacities in middle or lower lobes, or hilar or paratracheal lymphadenopathy, and/or pleural effusion.<br>• Sputum acid-fast bacilli smear and sputum culture: positive.<br>• Molecular testing: positive for *Mycoplasma tuberculosis* . |



# Diagnostic criteria

## World Health Organization: case definitions for surveillance[77]

Suspect case

- A. Patients with acute respiratory illness (i.e., fever and at least one sign/symptom of respiratory disease such as cough or shortness of breath) AND with no other aetiology that fully explains the clinical presentation AND a history of travel to or residence in a country/area or territory reporting local transmission of COVID-19 disease during the 14 days prior to symptom onset; OR
- B. Patients with any acute respiratory illness AND having been in contact with a confirmed or probable COVID-19 case in the last 14 days prior to onset of symptoms; OR
- C. Patients with severe acute respiratory infection (i.e., fever and at least one sign/symptom of respiratory disease such as cough or shortness of breath) AND requiring hospitalisation AND with no other aetiology that fully explains the clinical presentation.

Probable case

- A suspect case for whom testing is inconclusive.

Confirmed case

- A person with laboratory confirmation of infection, irrespective of signs and symptoms.

[WHO: global surveillance for COVID-19 disease caused by human infection with novel coronavirus (COVID-19)]

## Centers for Disease Control and Prevention: criteria to guide evaluation of patients under investigation (PUI) for COVID-19[76]

Clinicians should use their judgement to determine whether a patient has signs and symptoms compatible with COVID-19 and whether the patient should be tested. Decisions on which patients receive testing should be based on the local epidemiology of COVID-19, as well as the clinical course of illness.

Most patients with confirmed COVID-19 have developed fever and/or symptoms of acute respiratory illness (e.g., cough, difficulty breathing). Epidemiological factors that may help guide decisions on whether to test include: any persons, including healthcare workers, who have had close contact with a laboratory-confirmed COVID-19 patient within 14 days of symptom onset, or a history of travel from affected geographical areas (international areas with sustained/ongoing transmission) within 14 days of symptom onset. [CDC: coronavirus disease 2019 information for travel]

Clinicians are strongly encouraged to test for other causes of respiratory illness, including infections such as influenza.

[CDC: criteria to guide evaluation of persons under investigation (PUI) for COVID-19]



 

# Step-by-step treatment approach

No specific treatments are known to be effective for COVID-19 yet; therefore, the mainstay of management is early recognition and optimised supportive care to relieve symptoms and to support organ function in more severe illness. Patients should be managed in a hospital setting where possible; however, home care may be suitable for selected patients with mild illness unless there is concern about rapid deterioration or an inability to promptly return to hospital if necessary.

Much of the information in this section is based on early evidence, analysis of case series and reports (mostly limited to hospitalised patients with pneumonia), and data from previous betacoronavirus infections such as severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). Consult local guidance for further detailed information as the situation is evolving rapidly.

## Infection prevention and control

Immediately isolate all suspected or confirmed cases in an area separate from other patients. Suspected cases should be given a mask and kept at least 1 metre (3 feet) from other suspected cases. Implement appropriate infection prevention and control procedures. COVID-19 is a notifiable disease; report all suspected and confirmed cases to your local health authorities.

Detailed guidance on infection prevention and control procedures are available from the World Health Organization (WHO) and the US Centers for Disease Control and Prevention (CDC):

- [WHO: infection prevention and control during health care when novel coronavirus (nCoV) infection is suspected]
- [CDC: interim infection prevention and control recommendations for patients with suspected or confirmed coronavirus disease 2019 (COVID-19) in healthcare settings]

WHO recommends that patients should remain in isolation for two weeks after symptoms disappear, and visitors should not be allowed until the end of this period.[108]

## Severe COVID-19

Promptly admit patients with pneumonia or acute respiratory distress to an appropriate healthcare facility and start supportive care depending on the clinical presentation. Patients with impending or established respiratory failure should be admitted to an intensive care unit. Approximately 14% of patients present with severe illness requiring oxygen therapy, and 5% present with critical illness requiring intensive care unit treatment.[15] The median time from onset of symptoms to hospital admission is reported to be approximately 7 days.[6] [8]

Older patients and/or those with underlying health conditions such as cardiovascular disease or diabetes have a higher risk of severe illness and mortality and should be admitted to a designated unit for close monitoring.[5]

Supportive therapies

- Oxygen and airway management: give supplemental oxygen at a rate of 5 L/minute to patients with severe acute respiratory infection and respiratory distress, hypoxaemia, or shock. Titrate flow rates to reach a target $SpO_2$ ≥94% during resuscitation.[5] Use a face mask with a reservoir bag (at 10-15 L/minute) if the patient is in critical condition. Once the patient is stable, the target $SpO_2$ is

>90% in children and non-pregnant adults, and ≥92% to 95% in pregnant women. Nasal prongs or a nasal cannula are preferred in young children.[5]

- Fluids: manage fluids conservatively in adults and children with severe acute respiratory infection when there is no evidence of shock as aggressive fluid resuscitation may worsen oxygenation.[5]
- Symptom relief: give an antipyretic/analgesic for the relief of fever and pain.[5] There have been media reports stating that non-steroidal anti-inflammatory drugs such as ibuprofen could worsen COVID-19. However, there is currently no strong evidence to support this, and the situation is being monitored closely. The European Medicines Agency recommends that you should consider all available treatment options in patients with COVID-19 according to each drug's product information and national treatment guidelines, although it notes that paracetamol is usually the first-line option in guidelines.[109] NHS UK recommends paracetamol as the drug of choice until there is more information available.[110] Ibuprofen is not recommended in pregnant women, especially in the third trimester, or children <6 months of age.
- Antimicrobials: start empirical antimicrobials to cover other potential bacterial pathogens that may cause respiratory infection according to local protocols. Give within 1 hour of initial patient assessment for patients with suspected sepsis. Choice of empirical antimicrobials should be based on the clinical diagnosis, and local epidemiology and susceptibility data. Consider treatment with a neuraminidase inhibitor until influenza is ruled out. De-escalate empirical therapy based on microbiology results and clinical judgement.[5] Some patients with severe illness may require continued antimicrobial therapy once COVID-19 has been confirmed depending on the clinical circumstances.

Monitoring

- Monitor patients closely for signs of clinical deterioration, such as rapidly progressive respiratory failure and sepsis, and immediately start general supportive care interventions as indicated (e.g., haemodialysis, vasopressor therapy, fluid resuscitation, ventilation, antimicrobials) as appropriate.[5]

Mechanical ventilation

- It is important to follow local infection prevention and control procedures to prevent transmission to healthcare workers.
- Intubation and mechanical ventilation are recommended in patients who are deteriorating and failing to respond to standard oxygen therapy. Endotracheal intubation should be performed by an experienced provider using airborne precautions. Young children, or adults who are obese or pregnant, may desaturate quickly during intubation and therefore require pre-oxygenation with 100% fraction of inspired oxygen ($FiO_2$) for 5 minutes.[5] Some patients may develop severe hypoxic respiratory failure, requiring a high fraction of inspired oxygen, and high air flow rates to match inspiratory flow demand. Patients may also have increased work of breathing, demanding positive pressure breathing assistance.
- High-flow nasal oxygen and non-invasive ventilation are recommended in select patients. Mechanically ventilated patients with acute respiratory distress syndrome should receive a lung-protective, low tidal volume/low inspiratory pressure ventilation strategy (lower targets are recommended in children). Those with persistent severe hypoxic failure should be considered



 

for prone ventilation (pregnant women may benefit from being placed in the lateral decubitus position).[5]

- The risk of treatment failure is high in patients with non-acutely reversible conditions, and there is also concern about nosocomial transmission with open ventilation systems and suboptimal non-invasive face mask or nasal pillow seals. More research to define the balance of benefits and risks to patients and health workers is needed.
- Some patients may require extracorporeal membrane oxygenation (ECMO) according to availability and expertise.[5]

Tailor the management of critical illness to the patient's comorbidities (e.g., decide which chronic therapies should be continued and which therapies should be temporarily stopped, monitor for drug-drug interactions). The American Heart Association, the American College of Cardiology, the Heart Failure Society of America, and the European Society of Cardiology Council on Hypertension recommend that patients with COVID-19 who have underlying hypertension, heart failure, or ischaemic heart disease should continue taking their ACE inhibitors or angiotensin-II receptor antagonists as there is no evidence to suggest that these drugs increase the risk of developing severe COVID-19 despite theoretical concerns of increased expression of ACE2 in these patients.[111] [112]

Implement standard interventions to prevent complications associated with critical illness.[5] Complications such as acute respiratory distress syndrome (ARDS), sepsis, and septic shock should be managed according to usual protocols. See our Complications section for more information.

Symptomatic patients who no longer require hospitalisation may be considered for home care if suitable (see below).

## Mild COVID-19

Patients do not require hospital admission; however, isolation is necessary to contain transmission of the virus. Patients can be isolated in a hospital setting if there are only sporadic cases or small clusters, in repurposed non-traditional settings, or at home. Home care may be considered on a case-by-case basis. The decision will depend on guidance from local health authorities and resources. Forced quarantine orders are being used in some countries. Symptomatic treatment and monitoring is recommended in these patients. Advise patients to seek urgent care if they develop signs or symptoms of complicated disease.[5] [106]

Patients suitable for home care

- Mild symptoms only (e.g., low-grade fever, cough, fatigue, rhinorrhoea, sore throat).
- No warning signs (e.g., shortness of breath or difficulty breathing, haemoptysis, increased sputum production, gastrointestinal symptoms, mental status changes).
- No underlying health conditions.

Home infection prevention and control measures

- Infection prevention and control procedures are still important during home care. Recommend patients use a single room and a single bathroom (if possible), minimise contact with other household members, and wear a surgical mask if contact is necessary.[106]

- At this time, there is no evidence that pets and other animals can spread COVID-19. However, patients in home isolation should be advised to limit their interaction, and avoid direct contact with their pets and other animals, especially while they are symptomatic.[113]

Supportive therapies

- Recommend symptomatic therapies such as an antipyretic/analgesic, and advise patients to keep hydrated but not to take too much fluid as this can worsen oxygenation.[106]

Monitoring

- Monitor patients closely and advise them to seek medical care if symptoms worsen as mild illness can rapidly progress to lower respiratory tract disease.

More detailed guidance on home care is available from the WHO and the CDC:

- [WHO: home care for patients with suspected novel coronavirus (COVID-19) infection presenting with mild symptoms, and management of their contacts]
- [CDC: interim guidance for implementing home care of people not requiring hospitalization for coronavirus disease 2019 (COVID-19)]

## Pregnancy and breastfeeding

Pregnant women should be managed by a multidisciplinary team, including obstetric, perinatal, neonatal, and intensive care specialists, as well as mental health and psychosocial support. There is no evidence to suggest that pregnant women present with increased risk of severe illness or fetal compromise. Data on pregnant women with COVID-19 are limited; however, pregnant women can generally be treated with the same supportive therapies detailed above, taking into account the physiological changes that occur with pregnancy.[5]

Location of care

- Manage symptomatic pregnant women with confirmed infection in a hospital setting with appropriate maternal and fetal monitoring; women with severe illness or complications may require admission to an intensive care unit.[40]
- Isolate and monitor asymptomatic pregnant women with confirmed infection at home, if appropriate, with ultrasound fetal surveillance every 2 weeks.[40]

Delivery

- Choice of delivery and timing should be individualised based on gestational age, as well as maternal, fetal, and delivery conditions. Induction of labour and vaginal delivery is preferred in pregnant women with confirmed COVID-19 infection to avoid unnecessary surgical complications; however, an emergency caesarean delivery may be required if medically justified (e.g., in patients with complications such as sepsis or if there is fetal distress).[5] [40]
- Corticosteroid therapy may be considered in women who are at risk of preterm birth from 24 to 37 weeks' gestation for fetal lung maturation.[5] [40]

Newborns and breastfeeding

- Babies born to mothers with suspected or confirmed infection should be tested after birth.



 

- The WHO recommends that mothers and infants should remain together when possible, and 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).[5] However, the CDC recommends that temporary separation of the mother and baby should be considered on a case-by-case basis, at least until the mother's transmission-based precautions are discontinued. It recommends that mothers who intend to breastfeed should be encouraged to express their breast milk using a dedicated breast pump and using appropriate infection prevention and control measures in order to maintain milk supply. Expressed milk should be fed to the newborn by a healthy carer.[114] Consult local guidelines for specific recommendations.

### Experimental therapies

Drug therapies (e.g., antivirals) are being used in patients with COVID-19; however, unlicensed or experimental treatments should only be administered in the context of ethically-approved clinical trials.[5] See the Emerging section for more information about these treatments.

### Corticosteroids

Corticosteroids are being used in some patients with COVID-19; however, they have been found to be ineffective and are not recommended.[6] [115] The WHO (as well as other international pneumonia guidelines) do not routinely recommend systemic corticosteroids for the treatment of viral pneumonia or acute respiratory distress syndrome unless they are indicated for another reason.[5] A randomised controlled trial investigating the use of corticosteroids in patients with COVID-19 is in progress.[116]

## 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

| Initial | | ( summary ) |
|---|---|---|
| **suspected COVID-19** | | |
| | **1st** | **infection prevention and control procedures** |
| | **plus** | **supportive care plus monitoring** |
| | **plus** | **empirical antimicrobials** |

## Acute ( summary )

**confirmed COVID-19**

| | | |
|---|---|---|
| **severe illness** | **1st** | **hospital admission and infection prevention and control procedures** |
| | **plus** | **supportive care plus monitoring** |
| | **adjunct** | **mechanical ventilation** |
| | **adjunct** | **experimental therapies** |
| **mild illness** | **1st** | **consider home care and isolation** |
| | **plus** | **supportive care plus monitoring** |

# 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

# Initial

## suspected COVID-19

**1st** **infection prevention and control procedures**

» Immediately isolate all suspected cases in an area separate from other patients, and implement appropriate infection prevention and control procedures. Suspected cases should be given a mask and kept at least 1 metre (3 feet) from other suspected cases. Detailed guidance is available from the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC):

» [WHO: infection prevention and control during health care when novel coronavirus (nCoV) infection is suspected]

» [CDC: interim infection prevention and control recommendations for patients with suspected or confirmed coronavirus disease 2019 (COVID-19) in healthcare settings]

» COVID-19 is a notifiable disease; report all suspected cases to your local health authorities.

**plus** **supportive care plus monitoring**

Treatment recommended for ALL patients in selected patient group

» Immediately start supportive care based on the clinical presentation.

» Oxygen and airway management: give supplemental oxygen at a rate of 5 L/minute to patients with severe acute respiratory infection and respiratory distress, hypoxaemia, or shock. Titrate flow rates to reach a target $SpO_2$ ≥94% during resuscitation. Use a face mask with a reservoir bag (at 10-15 L/minute) if the patient is in critical condition. Once the patient is stable, the target $SpO_2$ is >90% in children and non-pregnant adults, and ≥92% to 95% in pregnant women. Nasal prongs or a nasal cannula are preferred in young children.[5]

» Fluids: manage fluids conservatively in adults and children with severe acute respiratory infection when there is no evidence of shock as aggressive fluid resuscitation may worsen oxygenation.[5]

» Symptom relief: give an antipyretic/analgesic for the relief of fever and pain.[5] There have been media reports stating that non-steroidal anti-inflammatory drugs such as ibuprofen could worsen COVID-19. However, there is



 

## Initial

currently no strong evidence to support this, and the situation is being monitored closely. The European Medicines Agency recommends that you should consider all available treatment options in patients with COVID-19 according to each drug's product information and national treatment guidelines, although notes that paracetamol is usually the first-line option in guidelines.[109] NHS UK recommends paracetamol as the drug of choice until there is more information available.[110] Ibuprofen is not recommended in pregnant women, especially in the third trimester, or children <6 months of age.

» Monitor patients closely for signs of clinical deterioration, such as rapidly progressive respiratory failure and sepsis, and immediately start general supportive care interventions as indicated (e.g., haemodialysis, vasopressor therapy, fluid resuscitation, ventilation, antimicrobials) as appropriate.[5]

» Pregnant women should be managed by a multidisciplinary team, including obstetric, perinatal, neonatal, and intensive care specialists, as well as mental health and psychosocial support.[5] [40]

**plus** **empirical antimicrobials**

Treatment recommended for ALL patients in selected patient group

» Start empirical antimicrobials to cover other potential bacterial pathogens that may cause respiratory infection according to local protocols. Give within 1 hour of initial patient assessment for patients with suspected sepsis. Choice of empirical antimicrobials should be based on the clinical diagnosis, and local epidemiology and susceptibility data.[5]

» Consider treatment with a neuraminidase inhibitor until influenza is ruled out.[5]

» De-escalate empiric therapy based on microbiology results and clinical judgement.

# Acute

## confirmed COVID-19

**severe illness**

**1st** **hospital admission and infection prevention and control procedures**

» Promptly admit patients with pneumonia or acute respiratory distress to an appropriate healthcare facility. Patients with impending or established respiratory failure should be admitted to an intensive care unit.

» Older patients and/or those with underlying health conditions such as cardiovascular disease or diabetes have a higher risk of severe illness and mortality and should be admitted to a designated unit for close monitoring.[5]

» Symptomatic pregnant women with confirmed infection should be managed in a hospital setting with appropriate maternal and fetal monitoring; women with severe illness or complications may require admission to an intensive care unit.[40]

» Immediately isolate all confirmed cases in an area separate from other patients, and implement appropriate infection prevention and control procedures. Detailed guidance is available from the WHO and the CDC:

» [WHO: infection prevention and control during health care when novel coronavirus (nCoV) infection is suspected]

» [CDC: interim infection prevention and control recommendations for patients with suspected or confirmed coronavirus disease 2019 (COVID-19) in healthcare settings]

» COVID-19 is a notifiable disease; report all confirmed cases to your local health authorities.

» Consider home care, if suitable, in symptomatic patients who no longer require hospitalisation.

» WHO recommends that patients should remain in isolation for two weeks after symptoms disappear, and visitors should not be allowed until the end of this period.[108]

**plus** **supportive care plus monitoring**

Treatment recommended for ALL patients in selected patient group

» Immediately start supportive care.

» Oxygen and airway management: give supplemental oxygen at a rate of 5 L/minute to

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patients with severe acute respiratory infection and respiratory distress, hypoxaemia, or shock. Titrate flow rates to reach a target $SpO_2$ ≥94% during resuscitation. Use a face mask with a reservoir bag (at 10-15 L/minute) if the patient is in critical condition. Once the patient is stable, the target $SpO_2$ is >90% in children and non-pregnant adults, and ≥92% to 95% in pregnant women. Nasal prongs or a nasal cannula are preferred in young children.[5]

» Fluids: manage fluids conservatively in adults and children with severe acute respiratory infection when there is no evidence of shock as aggressive fluid resuscitation may worsen oxygenation.[5]

» Symptom relief: give an antipyretic/analgesic for the relief of fever and pain.[5] There have been media reports stating that non-steroidal anti-inflammatory drugs such as ibuprofen could worsen COVID-19. However, there is currently no strong evidence to support this, and the situation is being monitored closely. The European Medicines Agency recommends that you should consider all available treatment options in patients with COVID-19 according to each drug's product information and national treatment guidelines, although notes that paracetamol is usually the first-line option in guidelines.[109] NHS UK recommends paracetamol as the drug of choice until there is more information available.[110] Ibuprofen is not recommended in pregnant women, especially in the third trimester, or children <6 months of age.

» Monitor patients closely for signs of clinical deterioration, such as rapidly progressive respiratory failure and sepsis, and immediately start general supportive care interventions as indicated (e.g., haemodialysis, vasopressor therapy, fluid resuscitation, ventilation, antimicrobials) as appropriate.[5]

» Tailor the management of critical illness to the patient's comorbidities (e.g., decide which chronic therapies should be continued and which therapies should be temporarily stopped, monitor for drug-drug interactions). The American Heart Association, the American College of Cardiology, the Heart Failure Society of America, and the European Society of Cardiology Council on Hypertension recommend that patients with COVID-19 who have underlying hypertension, heart failure, or ischaemic heart disease should continue taking their ACE inhibitors or angiotensin-II receptor antagonists as there is no evidence to suggest that these drugs increase

## Acute

the risk of developing severe COVID-19 despite theoretical concerns of increased expression of ACE2 in these patients.[111] [112]

» Implement standard interventions to prevent complications associated with critical illness.[5]

» Patients with severe illness may require continued antimicrobial therapy once COVID-19 has been confirmed depending on the clinical circumstances.

» Pregnant women should be managed by a multidisciplinary team, including obstetric, perinatal, neonatal, and intensive care specialists, as well as mental health and psychosocial support.[5] [40]

**adjunct** **mechanical ventilation**

Treatment recommended for SOME patients in selected patient group

» Intubation and mechanical ventilation are recommended in patients who are deteriorating and failing to respond to standard oxygen therapy.[5] Some patients may develop severe hypoxic respiratory failure, requiring a high fraction of inspired oxygen, and high air flow rates to match inspiratory flow demand. Patients may also have increased work of breathing, demanding positive pressure breathing assistance.

» Endotracheal intubation should be performed by an experienced provider using airborne precautions. Young children, or adults who are obese or pregnant, may desaturate quickly during intubation and therefore require pre-oxygenation with 100% fraction of inspired oxygen ($FiO_2$) for 5 minutes.[5]

» High-flow nasal oxygen and non-invasive ventilation are recommended in select patients. Mechanically ventilated patients with acute respiratory distress syndrome should receive a lung-protective, low tidal volume/low inspiratory pressure ventilation strategy (lower targets are recommended in children). Those with persistent severe hypoxic failure should be considered for prone ventilation (pregnant women may benefit from being placed in the lateral decubitus position).[5]

» The risk of treatment failure is high in patients with non-acutely reversible conditions, and there is also concern about nosocomial transmission with open ventilation systems and suboptimal non-invasive face mask or nasal pillow seals.



 

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More research to define the balance of benefits and risks to patients and health workers is needed.

» Some patients may require extracorporeal membrane oxygenation (ECMO) according to availability and expertise.[5]

» It is important to follow local infection prevention and control procedures to prevent transmission to healthcare workers.

**adjunct** **experimental therapies**

Treatment recommended for SOME patients in selected patient group

» Consider using experimental drug therapies. Antivirals and other drugs are being used in patients with COVID-19; however, unlicensed or experimental treatments should only be administered in the context of ethically-approved clinical trials.[5] See the Emerging section for more information about these treatments.

**mild illness** **1st** **consider home care and isolation**

» Patients do not require hospital admission; however, isolation is necessary to contain transmission of the virus. Patients can be isolated in a hospital setting if there are only sporadic cases or small clusters, in repurposed non-traditional settings, or at home.[5]

» Consider home care in patients who have mild symptoms only (e.g., low-grade fever, cough, fatigue, rhinorrhoea, sore throat), with no warning signs (e.g., shortness of breath or difficulty breathing, haemoptysis, increased sputum production, gastrointestinal symptoms, mental status changes), and no underlying health conditions.[106] Otherwise, hospital admission is required.

» Asymptomatic pregnant women with confirmed infection can be managed at home, if appropriate.[40]

» Infection prevention and control procedures are still important during home care. Recommend patients use a single room and a single bathroom (if possible), minimise contact with other household members, and wear a surgical mask if contact is necessary.[106]

» At this time, there is no evidence that pets can spread COVID-19. However, patients in home isolation should be advised to limit their interaction, and avoid direct contact with pets

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and other animals, especially while they are symptomatic.[113]

» More detailed guidance on home care is available from the WHO and the CDC:

» [WHO: home care for patients with suspected novel coronavirus (COVID-19) infection presenting with mild symptoms, and management of their contacts]

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

» The location of home care may depend on guidance from local health authorities and resources; forced quarantine orders are being used in some countries.

» WHO recommends that patients should remain in isolation for two weeks after symptoms disappear, and visitors should not be allowed until the end of this period.[108]

**plus** **supportive care plus monitoring**

Treatment recommended for ALL patients in selected patient group

» Recommend symptomatic therapies such as an antipyretic/analgesic, and advise patients to keep hydrated but not to take too much fluid as this can worsen oxygenation.[106]

» There have been media reports stating that non-steroidal anti-inflammatory drugs such as ibuprofen could worsen COVID-19. However, there is currently no strong evidence to support this, and the situation is being monitored closely. The European Medicines Agency recommends that you should consider all available treatment options in patients with COVID-19 according to each drug's product information and national treatment guidelines, although notes that paracetamol is usually the first-line option in guidelines.[109] Ibuprofen is not recommended in pregnant women, especially in the third trimester, or children <6 months of age.

» Monitor patients closely and advise them to seek medical care if symptoms worsen as mild illness can rapidly progress to lower respiratory tract disease.

» Ultrasound fetal surveillance is recommended every 2 weeks in pregnant women.[40]



 

# Emerging

## Antivirals

Various antivirals (monotherapy and combination therapy) are being trialled in patients with COVID-19 (e.g., oseltamivir, lopinavir/ritonavir, ganciclovir, favipiravir, baloxavir marboxil, umifenovir, ribavirin, interferon alfa); however, there are no data to support their use.[6] [7] [8] [117] [118] [119] [120] [121] [122] [123] [124] Results from one small case series found that evidence of clinical benefit with lopinavir/ritonavir was equivocal.[125] A randomised controlled trial of approximately 200 patients in China found that treatment with lopinavir/ritonavir was not beneficial compared with standard care alone (primary outcome was time to improvement) in hospitalised patients with severe COVID-19.[126] Remdesivir shows in vitro activity against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and has been used to treat patients in China, as well as the first patient in the US.[127] [128] Clinical trials with remdesivir have started in the US and in China.[129] [130] [131]

## Intravenous immunoglobulin

Intravenous immunoglobulin is being trialled in some patients with COVID-19; however, there are no data to support this.[7]

## Chloroquine and hydroxychloroquine

Chloroquine and hydroxychloroquine are being trialled in some patients with COVID-19.[132] [133] [134] Chloroquine shows in vitro activity against SARS-CoV-2.[128] [135] An expert consensus guideline in China recommends chloroquine in mild to severe cases of COVID-19 as it may improve the success rate of treatment, shorten hospital stay, and improve patient outcome.[136]

## Traditional Chinese Medicine

Traditional Chinese Medicine is being trialled in some patients with COVID-19 (e.g., Xue-Bi-Jing, Shuang-Huang-Lian, Xin-Guan-2); however, there are no data to support this.[137] [138] [139] These medicines are commonly used in China to treat COVID-19 patients.[140]

## 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 pathological changes that occur in the lungs, and inhibit the cell-mediated immune inflammatory response.[141]

## 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.[142]

## Convalescent plasma

Convalescent plasma from patients who have recovered from viral infections has been used as a treatment in previous virus outbreaks including SARS, avian influenza, and Ebola virus infection.[143] A clinical trial to determine the safety and efficacy of convalescent plasma in patients with COVID-19 has started in China; however, there is no data on its use as yet.[144]

## Other drugs

Other drugs that may show promise for the treatment of COVID-19 include teicoplanin and camostat mesylate.[145] [146]

# Recommendations

## Monitoring

Monitor vital signs (i.e., temperature, respiratory rate, heart rate, blood pressure, oxygen saturation) and perform haematology and biochemistry laboratory testing and ECG as clinically indicated during admission. Utilise medical early warning scores that facilitate early recognition and escalation of treatment of deteriorating patients (e.g., National Early Warning Score 2 [NEWS2]) where possible.[5]

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.[40]

Perform molecular testing regularly during admission. Two consecutive negative tests (at least 24 hours apart) are required in a clinically recovered patient before discharge.[5] However, there is a case report of a patient who tested positive again after two consecutive negative results two days apart, even though they had no longer had a fever and their respiratory symptoms had improved. This suggests that some patients in convalescence may still be contagious.[159]

## Patient instructions

General prevention measures

- Wash hands often with soap and water or an alcohol-based hand sanitiser and avoid touching the eyes, nose, and mouth with unwashed hands.
- Avoid close contact with people (i.e., maintain a distance of at least 1 metre [3 feet]), particularly those who are sick.
- Stay at home if sick and isolate yourself from other people.
- Practice respiratory hygiene (i.e., cover mouth and nose when coughing or sneezing, discard tissue immediately in a closed bin, and wash hands).
- Regularly clean and disinfect frequently touched objects and surfaces.[59] [60]
- [WHO: coronavirus disease (COVID-19) advice for the public]

Travel advice

- Many countries have implemented international travel bans and have issued advice for domestic travel. 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.
- The World Health Organization (WHO) continues to advise against any travel or trade restrictions to countries experiencing outbreaks (as of 27 February 2020). However, they do recommend that international travellers who are sick should delay or avoid travel to affected areas, especially older people or people with underlying health conditions or chronic diseases. Usual precautions (e.g., frequent hand hygiene, cough etiquette, keeping a distance of at least 1 metre [3 feet] from people showing symptoms, food hygiene practices) are important for all travellers. [WHO: coronavirus disease (COVID-19) travel advice]
- In the US, the Centers for Disease Control and Prevention (CDC) recommends avoiding all non-essential travel to China (this does not include Hong Kong, Macau, or Taiwan), South Korea,

 

Malaysia, Iran, most European countries, the UK, and Ireland as these areas have widespread sustained ongoing transmission. They also recommend that older adults and those with chronic medical conditions should consider postponing non-essential travel to any global location. Entry of foreign nationals from China, Iran, most European countries, the UK, and Ireland has been suspended. [CDC: coronavirus disease 2019 (COVID-19): travel] The CDC recommends that all travelers, particularly older and adults and/or those with underlying health issues, defer all cruise ship travel worldwide.[160] The US Department of State has issued an advisory recommending that all Americans reconsider travel to all countries.[161]

Resources

- [WHO: coronavirus disease (COVID-19) outbreak]
- [CDC: coronavirus disease 2019 (COVID-19)]
- [CDC: FAQ for healthcare professionals]

# Complications

| Complications | Timeframe | Likelihood |
|---|---|---|
| **acute respiratory distress syndrome (ARDS)** | **short term** | **medium** |
| Reported in 15% to 33% of patients in case series.[6] [7] [8] [79] [100]<br><br>Children can quickly progress to ARDS.[20]<br><br>Factors that increase the risk of developing ARDS and death include older age, neutrophilia, elevated lactate dehydrogenase level, and elevated D-dimer level. Treatment with methylprednisolone may be beneficial and decrease the risk of death in these patients.[153] | | |
| **acute liver injury** | **short term** | **medium** |
| Reported in 14% to 53% of patients in case series. Occurs more commonly in patients with severe disease.[154] | | |
| **acute cardiac injury** | **short term** | **low** |
| Reported in 7% to 13% of patients in case series.[6] [8] [100] Arrhythmias have been reported in 16% of patients in case series.[8]<br><br>Prevalence is high among patients who are severely or critically ill, and these patients have a higher rate of in-hospital mortality.[155]<br><br>Fulminant myocarditis has been reported.[152] Early corticosteroid therapy and immunoglobulin may be beneficial in these patients.[156]<br><br>Infection may have longer-term implications for overall cardiovascular health; however, further research is required.[157] | | |
| **secondary infection** | **short term** | **low** |
| Reported in 6% to 10% of patients in case series.[6] [100] | | |
| **acute respiratory failure** | **short term** | **low** |
| Reported in 8% of patients in case series.[7]<br><br>Leading cause of mortality in patients with COVID-19.[152]<br><br>Children can quickly progress to respiratory failure.[20] | | |
| **acute kidney injury** | **short term** | **low** |
| Reported in 3% to 8% of patients in case series.[6] [7] [100] | | |
| **septic shock** | **short term** | **low** |
| Reported in 4% to 8% of patients in case series.[6] [7] [8] [100]<br><br>A systemic inflammatory response syndrome (SIRS) can sometimes accompany viral sepsis. Elevations in inflammatory chemokines and cytokines have been reported in COVID-19 patients.[6] [158] | | |
| **disseminated intravascular coagulation** | **short term** | **low** |

 

| Complications | Timeframe | Likelihood |
|---|---|---|
| Reported in 71% of non-survivors.[102] | | |
| **pregnancy-related complications** | **short term** | **low** |
| Retrospective reviews of pregnant women with COVID-19 found that women appeared to have fewer adverse maternal and neonatal complications and outcomes than would be expected for those with severe acute respiratory syndrome (SARS) or Middle East respiratory syndrome (MERS). Adverse effects on the newborn including fetal distress, premature labour, respiratory distress, thrombocytopenia, and abnormal liver function have been reported; however, it is unclear whether these effects are related to maternal SARS-CoV-2 infection. No maternal deaths have been reported.[42] [43] [44] | | |

# Prognosis

Based on a large case series of patients in China (72,314 reported cases from 31 December 2019 to 11 February 2020), the overall case fatality rate is 2.3% (0.9% in patients without comorbidities). However, the majority of these cases were among hospitalised patients. The majority of deaths have been in patients aged 60 years and older and/or those who have pre-existing underlying health conditions (e.g., hypertension, diabetes, cardiovascular disease). The case fatality rate was highest among critical cases (49%). It was also higher in patients aged 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).[15] In the US, the case fatality rate was highest among patients aged ≥85 years (10% to 27%), followed by those aged 65 to 84 years (3% to 11%), 55 to 64 years (1% to 3%), 20 to 54 years (<1%), and ≤19 years (no deaths). Patients aged ≥65 years accounted for 80% of deaths.[19]

Based on World Health Organization data as of 18 March 2020, the case fatality rate appears to be higher in some countries. For example, in Italy, the country with the highest number of cases outside of China, the case fatality rate is 7.9%. In Iran, the country with the second highest number of cases outside of China, the case fatality rate is 6.1%. Globally, the case fatality rate is 4%.[147] However, it is important to note that estimated case fatality rates should be treated with extreme caution as the situation is evolving rapidly, and case fatality rates are often overestimated at the onset of outbreaks owing to increased case detection of patients with severe disease.[148]

The overall case fatality rate appears to be less than that reported for severe acute respiratory syndrome coronavirus (SARS) (10%) and Middle East respiratory syndrome (MERS) (37%).[6] Despite the lower case fatality rate, COVID-19 has so far resulted in more deaths than both SARS and MERS combined.[149]

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. Non-survivors were more likely to develop acute respiratory distress syndrome and require mechanical ventilation. Non-survivors were older (>65 years of age) and more likely to have chronic medical illnesses.[150]

Factors associated with disease progression and a poorer prognosis in one retrospective analysis of 78 patients in Wuhan City include older age, history of smoking, maximum body temperature on admission, respiratory failure, significantly decreased serum albumin level, and significantly elevated C-reactive protein.[151] Thrombocytopenia has been associated with increased risk of severe disease and mortality and may be useful as a clinical indicator for monitoring disease progression.[101] Other factors associated with a poor prognosis include higher Sequential Organ Failure Assessment (SOFA) score and a D-dimer level >1 microgram/L. Viral shedding continued until death in non-survivors.[56]

The leading cause of mortality is respiratory failure from acute respiratory distress syndrome.[152]

# Diagnostic guidelines

## Europe

### COVID-19: guidance for health professionals

**Published by:** Public Health England **Last published:** 2020

### COVID-19

**Published by:** European Centre for Disease Prevention and Control **Last published:** 2020

## International

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

**Published by:** World Health Organization **Last published:** 2020

### Laboratory testing for coronavirus disease 2019 (COVID-19) in suspected human cases

**Published by:** World Health Organization **Last published:** 2020

### Global surveillance for COVID-19 disease caused by human infection with novel coronavirus (COVID-19)

**Published by:** World Health Organization **Last published:** 2020

### Infection prevention and control during health care when novel coronavirus (nCoV) infection is suspected

**Published by:** World Health Organization **Last published:** 2020

## North America

### Information for laboratories

**Published by:** Centers for Disease Control and Prevention **Last published:** 2020

### Interim infection prevention and control recommendations for patients with suspected or confirmed coronavirus disease 2019 (COVID-19) in healthcare settings

**Published by:** Centers for Disease Control and Prevention **Last published:** 2020

### Interim US guidance for risk assessment and public health management of persons with potential coronavirus disease 2019 (COVID-19) exposures: geographic risk and contacts of laboratory-confirmed cases

**Published by:** Centers for Disease Control and Prevention **Last published:** 2020

## Asia

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

**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

**Published by:** Peking Union Medical College Hospital **Last published:** 2020

# Treatment guidelines

## Europe

### COVID-19: guidance for health professionals

**Published by:** Public Health England **Last published:** 2020

### Coronavirus (covid-19): latest news and resources

**Published by:** BMJ **Last published:** 2020

### COVID-19

**Published by:** European Centre for Disease Prevention and Control **Last published:** 2020

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

**Published by:** Spanish Paediatric Association **Last published:** 2020

## International

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

**Published by:** World Health Organization **Last published:** 2020

### Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected

**Published by:** World Health Organization **Last published:** 2020

### Home care for patients with suspected novel coronavirus (COVID-19) infection presenting with mild symptoms, and management of their contacts

**Published by:** World Health Organization **Last published:** 2020

### Advice on the use of masks in the community, during home care and in health care settings in the context of the novel coronavirus (2019-nCoV) outbreak

**Published by:** World Health Organization **Last published:** 2020

### ISUOG interim guidance on 2019 novel coronavirus infection during pregnancy and puerperium: information for healthcare professionals

**Published by:** International Society of Ultrasound in Obstetrics and Gynecology **Last published:** 2020

## North America

### Information for healthcare professionals

**Published by:** Centers for Disease Control and Prevention **Last published:** 2020

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

**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)

**Published by:** Centers for Disease Control and Prevention **Last published:** 2020

### Discontinuation of in-home isolation for immunocompromised persons with COVID-19 (interim guidance)

**Published by:** Centers for Disease Control and Prevention **Last published:** 2020

### Discontinuation of home isolation for persons with COVID-19 (interim guidance)

**Published by:** Centers for Disease Control and Prevention **Last published:** 2020

### Interim U.S. guidance for risk assessment and public health management of healthcare personnel with potential exposure in a healthcare setting to patients with coronavirus disease (COVID-19)

**Published by:** Centers for Disease Control and Prevention **Last published:** 2020

### Interim considerations for infection prevention and control of coronavirus disease 2019 (COVID-19) in inpatient obstetric healthcare settings

**Published by:** Centers for Disease Control and Prevention **Last published:** 2020

### Coronavirus disease (COVID-19): outbreak update

**Published by:** Government of Canada **Last published:** 2020

## Asia

### Coronavirus disease

**Published by:** Chinese Center for Disease Control and Prevention **Last published:** 2020

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

**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

**Published by:** Peking Union Medical College Hospital **Last published:** 2020

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

**Published by:** Ministry of Health Singapore **Last published:** 2020

### New coronavirus (COVID-19)#

**Published by:** National Institute of Infectious Diseases Japan **Last published:** 2020

### New coronavirus infection

**Published by:** Japanese Association for Infectious Diseases **Last published:** 2020

### Chinese expert consensus on the perinatal and neonatal management for the prevention and control of the 2019 novel coronavirus infection (first edition)

**Published by:** Working Committee on Perinatal and Neonatal Management for the Prevention and Control of the 2019 Novel Coronavirus Infection **Last published:** 2020

## Oceania

### Coronavirus disease 2019 (COVID-19)

**Published by:** Department of Health Australia **Last published:** 2020

# Online resources

1. WHO: novel coronavirus (COVID-19) situation dashboard *(external link)*
2. WHO: coronavirus disease (COVID-2019) situation reports *(external link)*
3. CDC: coronavirus disease 2019 (COVID-19) in the US *(external link)*
4. CDC: locations with confirmed COVID-19 cases, by WHO region *(external link)*
5. National Health Committee of the People's Republic of China: outbreak report *(external link)*
6. GenBank *(external link)*
7. WHO: coronavirus disease (COVID-19) advice for the public *(external link)*
8. BMJ: facemasks for the prevention of infection in healthcare and community settings *(external link)*
9. BMJ: covid-19 in primary care (UK) *(external link)*
10. WHO: infection prevention and control during health care when novel coronavirus (nCoV) infection is suspected *(external link)*
11. CDC: interim infection prevention and control recommendations for patients with suspected or confirmed coronavirus disease 2019 (COVID-19) in healthcare settings *(external link)*
12. WHO: global surveillance for COVID-19 disease caused by human infection with novel coronavirus (COVID-19) *(external link)*
13. CDC: coronavirus disease 2019 information for travel *(external link)*
14. CDC: criteria to guide evaluation of persons under investigation (PUI) for COVID-19 *(external link)*
15. WHO: home care for patients with suspected novel coronavirus (COVID-19) infection presenting with mild symptoms, and management of their contacts *(external link)*
16. CDC: interim guidance for implementing home care of people not requiring hospitalization for coronavirus disease 2019 (COVID-19) *(external link)*
17. WHO: coronavirus disease (COVID-19) travel advice *(external link)*
18. WHO: coronavirus disease (COVID-19) outbreak *(external link)*
19. CDC: coronavirus disease 2019 (COVID-19) *(external link)*
20. CDC: FAQ for healthcare professionals *(external link)*

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# Images

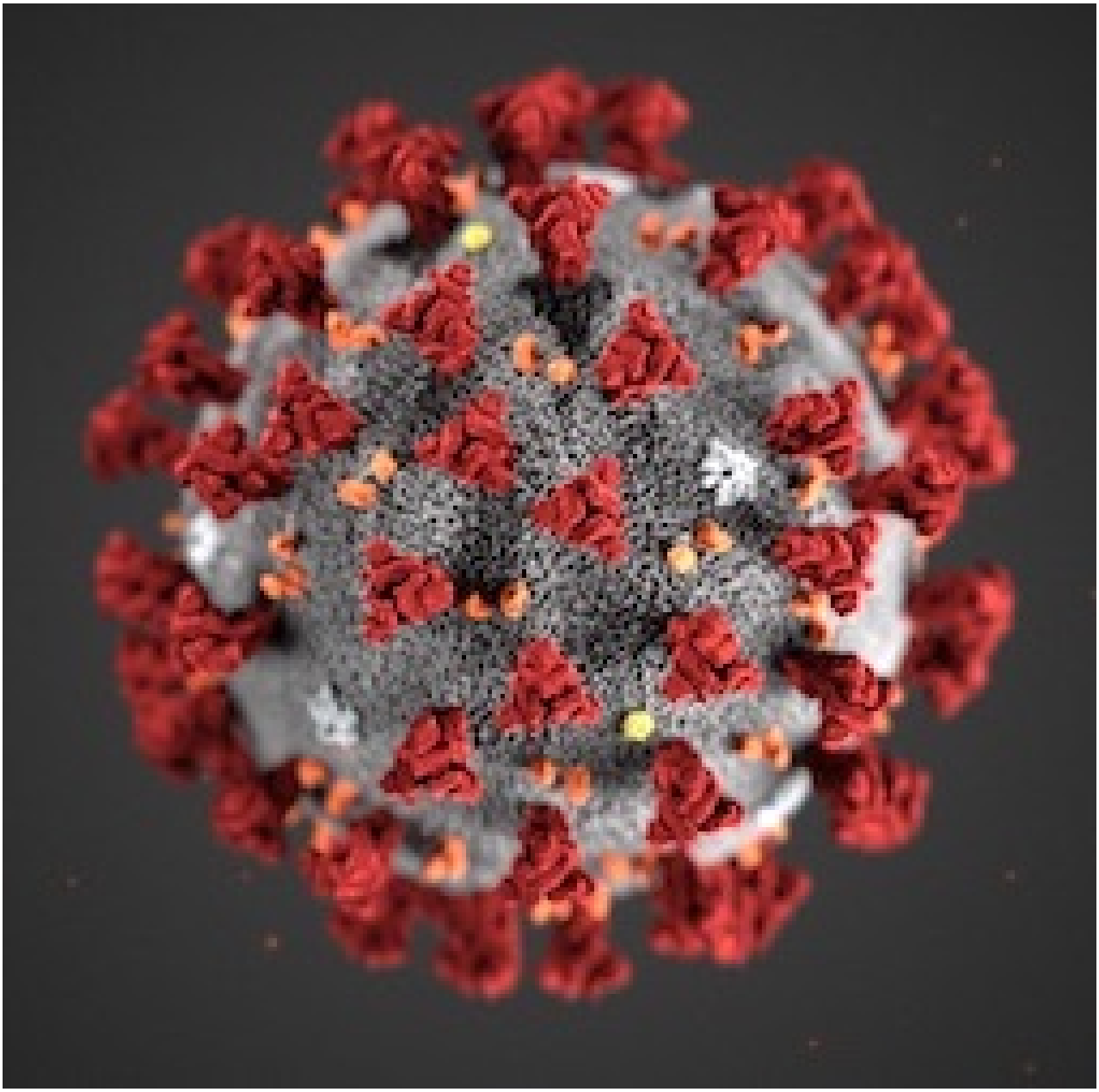

*Figure 1: Illustration revealing ultrastructural morphology exhibited by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) when viewed with electron microscopically*

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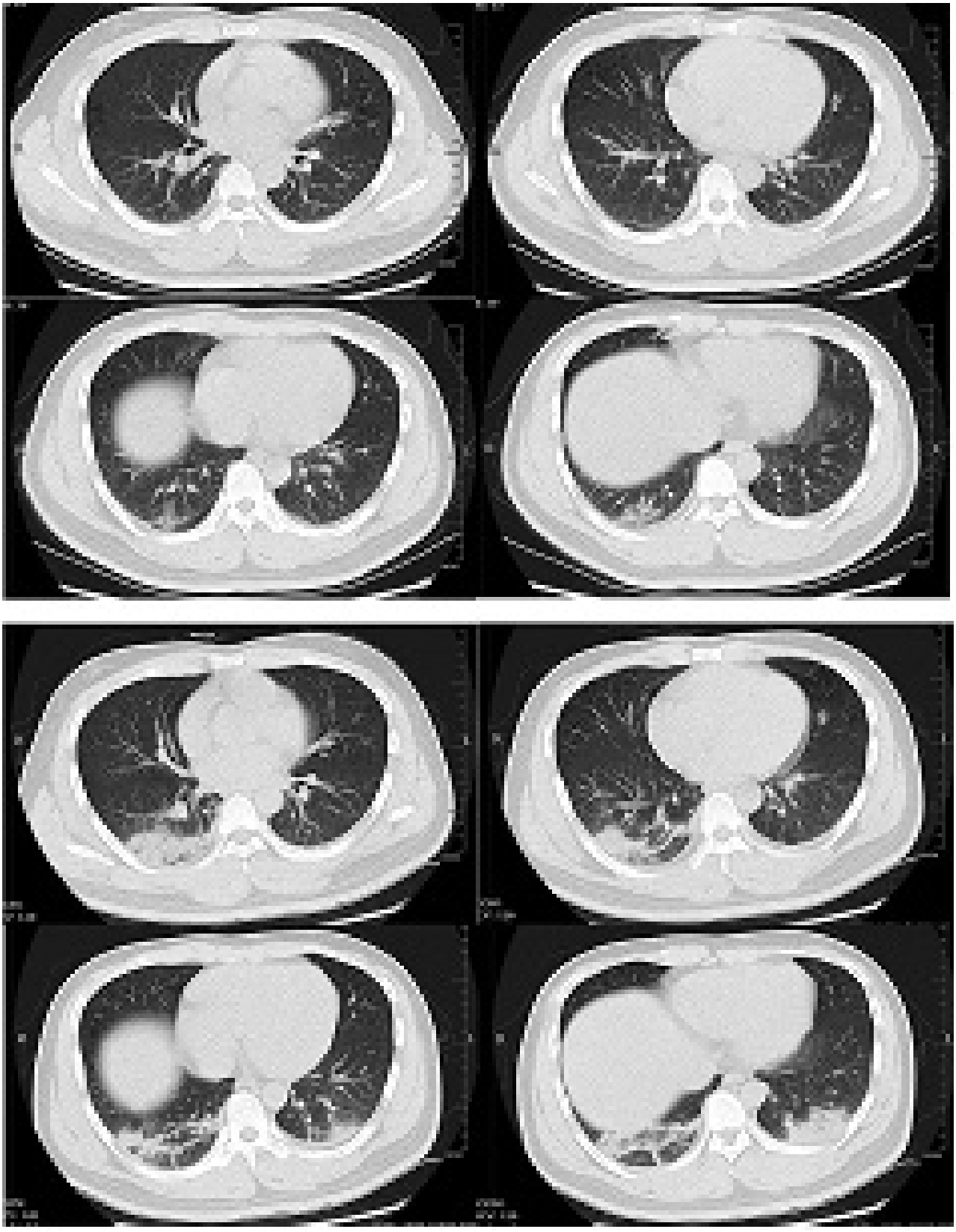

*Figure 2: Transverse CT scans from a 32-year-old man, showing ground-glass opacity and consolidation of lower lobe of right lung near the pleura on day 1 after symptom onset (top panel), and bilateral ground-glass opacity and consolidation on day 7 after symptom onset*

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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.