

Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19)

Summary of Recent Changes

Revisions were made on March 7, 2020, to reflect the following:

- Characteristics of patients with confirmed COVID-19 based on recent epidemiologic data from China, including characteristics of patients with COVID-19 admitted to the intensive care unit and data on pediatric cases
- Data regarding SARS-CoV-2 viral shedding among asymptomatic persons, and data from a recent report of viable SARS-CoV-2 isolation from stool
- Accessibility of investigational drug therapies for COVID-19 treatment through clinical trial enrollment in the United States
- Recently published pediatric surviving sepsis guidance

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Updated March 7, 2020

This interim guidance is for clinicians caring for patients with confirmed infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease (COVID-19).

This update includes additional information from recent reports including:

- Characteristics of patients with confirmed COVID-19 based on recent epidemiologic data from China, including characteristics of patients with COVID-19 admitted to the intensive care unit and data on pediatric cases
- Data regarding SARS-CoV-2 viral shedding among asymptomatic persons, and data from a recent report of viable SARS-CoV-2 isolation from stool
- Accessibility of investigational drug therapies for COVID-19 treatment through clinical trial enrollment in the United States
- Recently published pediatric surviving sepsis guidance

CDC will update this interim guidance as more information becomes available.

Clinical Presentation

Among reports that describe the clinical presentation of patients with confirmed COVID-19, most are limited to hospitalized patients with pneumonia. The incubation period is estimated at 4 days (interquartile range: 2 to 7 days). [1] Some studies have estimated a wider range for the incubation period; data for human infection with other coronaviruses (e.g. MERS-CoV, SARS-CoV) suggest that the incubation period may range from 2-14 days. Frequently reported signs and symptoms of patients admitted to the hospital include fever (77–98%), cough (46%–82%), myalgia or fatigue (11–52%), and shortness of breath (3–31%) at illness onset. [2–5] Among 1,099 hospitalized COVID-19 patients, fever was present in 44% at hospital admission, and developed in 89% during hospitalization. [6] Other less commonly reported respiratory symptoms include sore throat, headache, cough with sputum production and/or hemoptysis. Some patients have experienced gastrointestinal symptoms such as diarrhea and nausea prior to developing fever and lower respiratory tract signs and symptoms. The fever course among patients with COVID-19 is not fully understood; it may be prolonged and intermittent. A limited number

of reports describe identification of asymptomatic or subclinical infection on the basis of detection of SARS-CoV-2 RNA or live virus from throat swab specimens of contacts of confirmed patients. [7–8]

Risk factors for severe illness are not yet clear, although older patients and those with chronic medical conditions may be at higher risk for severe illness. Among more than 44,000 confirmed cases of COVID-19 in China as of Feb 11, 2020, most occurred among patients aged 30–69 years (77.8%), and approximately 19% were severely or critically ill [9]. Case-fatality proportion among cases aged ≥ 60 years was: 60–69 years: 3.6%; 70–79 years: 8%; ≥ 80 years: 14.8%. Patients who reported no underlying medical conditions had an overall case fatality of 0.9%, but case fatality was higher for patients with comorbidities: 10.5% for those with cardiovascular disease, 7% for diabetes, and 6% each for chronic respiratory disease, hypertension, and cancer. Case fatality for patients who developed respiratory failure, septic shock, or multiple organ dysfunction was 49%. [9]

Limited information is available about the clinical presentation, clinical course, and risk factors for severe COVID-19 in children. Of confirmed COVID-19 patients in China as of Feb 11, 2020, only 2.1% were aged < 20 years, and no deaths were reported among those < 10 years of age [9]. From limited published reports, signs and symptoms among children with COVID-19 may be more mild than adults, with most pediatric patients presenting with fever, cough, congestion, and rhinorrhea [10, 12–13], and one report of primarily gastrointestinal symptoms (vomiting and diarrhea) [13]. Prolonged detection of SARS-CoV RNA has been reported in respiratory specimens (up to 22 days after illness onset) and stool specimens (at least 30 days after illness onset) [10–11]. Severe complications of acute respiratory distress syndrome and septic shock were reported in a 13-month old with COVID-19 in China [13].

Clinical Course

Clinical presentation among reported cases of COVID-19 varies in severity from asymptomatic infection to mild illness to severe or fatal illness. Some reports suggest the potential for clinical deterioration during the second week of illness.[2,5] In one report, among patients with confirmed COVID-19 and pneumonia, just over half of

patients developed dyspnea a median of 8 days after illness onset (range: 5–13 days). [2] In another report, the mean time from illness onset to hospital admission with pneumonia was 9 days.[1] Acute respiratory distress syndrome (ARDS) developed in 17–29% of hospitalized patients, and secondary infection developed in 10%. [2,4] In one report, the median time from symptom onset to ARDS was 8 days.[3]

Approximately 20-30% of hospitalized patients with COVID-19 and pneumonia have required intensive care for respiratory support.[2–3] Compared to patients not admitted to an intensive care unit, critically ill patients were older (median age 66 years versus 51 years), and were more likely to have underlying co-morbid conditions (72% versus 37%). [3] Among critically ill patients admitted to an intensive care unit, 11–64% received high-flow oxygen therapy and 47-71% received mechanical ventilation; some hospitalized patients have required advanced organ support with endotracheal intubation and mechanical ventilation (4–42%).[3–4,9] A small proportion have also been supported with extracorporeal membrane oxygenation (ECMO, 3–12%).[3–4,9] Other reported complications include cardiac injury, arrhythmia, septic shock, liver dysfunction, acute kidney injury, and multi-organ failure. Post-mortem biopsies in one patient who died of ARDS reported pulmonary findings of diffuse alveolar damage. [14]

An overall case fatality proportion of 2.3% has been reported among confirmed cases of COVID-19 in China. [9] However, the majority of these cases were among hospitalized patients and therefore this estimate of mortality is likely biased upward. Among hospitalized patients with pneumonia, the case fatality proportion has been reported as 4–15%.[2–4] Among critically ill COVID-19 patients in China, the reported case fatality proportion was 49%. In a report from one hospital, 61.5% of critically ill patients with COVID-19 had died by day 28 of ICU admission. [9,15]

Diagnostic Testing

Information on specimen collection, handling, and storage is available at: [Real-Time RT-PCR Panel for Detection 2019-Novel Coronavirus](#). After initial confirmation of COVID-10, additional testing of clinical specimens can help inform clinical management, including discharge planning.

Laboratory and Radiographic Findings

The most common laboratory abnormalities reported among hospitalized patients with pneumonia on admission included leukopenia (9–25%), leukocytosis (24–30%), lymphopenia (63%), and elevated alanine aminotransferase and aspartate aminotransferase levels (37%). [2,4] Among 1,099 COVID-19 patients, lymphocytopenia was present in 83%; 36% had thrombocytopenia, and 34% had leukopenia. [6] Most patients had normal serum levels of procalcitonin on admission. Chest CT images have shown bilateral involvement in most patients. Multiple areas of consolidation and ground glass opacities are typical findings reported to date. [2–4, 16–24] However, one study that evaluated the time from symptom onset to initial CT scan found that 56% of patients who presented within 2 days had a normal CT. [20]

Limited data are available about the detection of SARS-CoV-2 RNA and infectious virus in clinical specimens. SARS-CoV-2 RNA has been detected from upper and lower respiratory tract specimens, and the virus has been isolated in cell culture from upper respiratory tract specimens and bronchoalveolar lavage fluid. In one case series SARS-CoV-2 viral RNA levels in the first 3 days after symptom onset were higher in specimens collected from the nose than from the throat (as demonstrated by lower cycle threshold values in the nose). [25] A similar time course and pattern of viral RNA detection was reported in one asymptomatic patient after exposure to a patient with confirmed COVID-19. [25]

SARS-CoV-2 RNA has been detected in blood and stool specimens and SARS-CoV-2 virus has been isolated in cell culture from the stool of a patient with pneumonia 15 days after symptom onset. [26–29]. The duration of SARS-CoV-2 RNA detection in the upper and lower respiratory tracts and in extrapulmonary specimens is not yet known. It is possible that RNA could be detected for weeks, which has occurred in some cases of MERS-CoV or

SARS-CoV infection. [30–37] Viable SARS-CoV has been isolated from respiratory, blood, urine, and stool specimens. In contrast, viable MERS-CoV has been isolated only from respiratory tract specimens. [37–39]

Clinical Management and Treatment

For information regarding infection prevention and control recommendations, please see [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](#).

Patients with a mild clinical presentation may not initially require hospitalization. However, clinical signs and symptoms may worsen with progression to lower respiratory tract disease in the second week of illness; all patients should be monitored closely. Possible risk factors for progressing to severe illness may include, but are not limited to, older age, and underlying chronic medical conditions such as lung disease, cancer, heart failure, cerebrovascular disease, renal disease, liver disease, diabetes, immunocompromising conditions, and pregnancy.

The decision to monitor a patient in the inpatient or outpatient setting should be made on a case-by-case basis. This decision will depend not only on the clinical presentation, but also on the patient's ability to engage in monitoring, home isolation, and the risk of transmission in the patient's home environment. For more information, see [Evaluating and Reporting Persons Under Investigation \(PUI\)](#)

No specific treatment for COVID-19 is currently available. Clinical management includes prompt implementation of recommended infection prevention and control measures and supportive management of complications, including advanced organ support if indicated.

Corticosteroids should be avoided, because of the potential for prolonging viral replication as observed in MERS-CoV patients, unless indicated for other reasons. [31, 40–42] For example, for a chronic obstructive pulmonary disease exacerbation or for septic shock per Surviving Sepsis guidelines for [adultsexternal icon](#) and [childrenexternal icon](#).

For more information, see: [WHO interim guidance on clinical management of severe acute respiratory infection when novel coronavirus \(nCoV\) infection is suspected](#)[external icon](#), [Diagnosis and Treatment of Adults with Community-acquired Pneumonia. An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America](#)[external icon](#), and [Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children](#)[external icon](#)

Investigational Therapeutics

There are currently no antiviral drugs licensed by the U.S. Food and Drug Administration (FDA) to treat patients with COVID-19. In the United States, the National Institutes of Health (NIH) and collaborators are working on development of candidate vaccines and therapeutics for COVID-19. Some in-vitro or in-vivo studies suggest potential therapeutic activity of compounds against related coronaviruses, but there are no available data from randomized controlled trials in humans to support recommending any investigational therapeutics for patients with confirmed or suspected COVID-19 at this time.

Remdesivir is an investigational antiviral drug that was reported to have in-vitro activity against SARS-CoV-2. [43] Some patients with COVID-19 have received intravenous remdesivir for compassionate use outside of a clinical trial setting. In China, multiple clinical trials of investigational therapeutics have been implemented, including two clinical trials of remdesivir. An [NIH adaptive randomized controlled clinical trial](#) [external icon](#) of investigational therapeutics for hospitalized COVID-19 patients in the United States was approved by the Food and Drug Administration; the first investigational therapeutic to be studied is remdesivir. Other remdesivir trials for COVID-19 patients in the U.S. are available (participants with [severe](#)[external icon](#) and [moderate](#)[external icon](#) coronavirus disease). Some COVID-19 patients have received uncontrolled treatment with other investigational antivirals. [4, 28, 44] For information on specific clinical trials underway for treatment of patients with COVID-19, see [clinicaltrials.gov](#)[external icon](#), and [www.chictr.org.cn](#)[external icon](#)

In the absence of an approved vaccine, community mitigation measures are the primary way to reduce SARS-CoV-2 transmission among persons in the community, and adherence to recommended infection prevention and control measures can reduce the risk of SARS-CoV-2 spread in healthcare facilities. In the absence of an approved therapeutic with demonstrated safety and efficacy in patients with COVID-19, clinical management of COVID-19 patients includes avoidance of corticosteroids, and supportive care of complications, including advanced organ support.

Discontinuation of Transmission-Based Precautions or Home Isolation

For recommendations on discontinuation of transmission-based precautions or home isolation for patients who have recovered from COVID-19 illness, please see: [Interim Guidance for Discontinuation of Transmission-Based Precautions and Disposition of Hospitalized Patients with COVID-19](#) and [Interim Guidance for Discontinuation of In-Home Isolation for Patients with COVID-19](#)

Additional resources:

- [Evaluating and Reporting Persons Under Investigation \(PUI\)](#)
- [Resources for Hospitals and Healthcare Professionals Preparing for Patients with Suspected or Confirmed COVID-19](#)
- [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](#)
- [World Health Organization. Interim Guidance on Clinical management of severe acute respiratory infection when novel coronavirus \(nCoV\) infection is suspected](#)[external icon](#)
- [American Thoracic Society and Infectious Diseases Society of America Clinical Practice Guidelines. Diagnosis and treatment of adults with community-acquired pneumonia](#)[external icon](#)
- [Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016](#)[external icon](#)

- [Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children](#)^{external icon}
- [Clinical Practice Guidelines by the Infectious Diseases Society of America: 2018 Update on Diagnosis, Treatment, Chemoprophylaxis, and Institutional Outbreak Management of Seasonal Influenza](#)^{external icon}

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