

**REVIEWED***By Chris at 9:58 am, May 01, 2020*

# Coronavirus Disease 2019 (COVID-19)

## Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease 2019 (COVID-19)

### Summary of Recent Changes

Revisions were made on April 3, 2020, to reflect the following:

- New information about asymptomatic and pre-symptomatic infections
- Non-steroidal anti-inflammatory drugs, angiotensin-converting enzyme inhibitors, and beta-blockers and risk of infection or infection severity
- Information about COVID-19 and potential for SARS-CoV-2 reinfection
- Possibility of infection with both SARS-CoV-2 and other respiratory viruses
- Additional laboratory and imaging findings in COVID-19
- Updated guidelines from the World Health Organization and the Surviving Sepsis Campaign
- Inclusion of new resource: [Information for Clinicians on Therapeutic Options for COVID-19](#)
- Inclusion of [National Institutes of Health: Coronavirus Disease 2019 \(COVID-19\) Treatment Guidelines](#)

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 2019 (COVID-19). Clinical guidance as more information becomes available.

The National Institutes of Health recently published guidelines on prophylaxis use, testing, and treatment of patients. For more information, please visit: [National Institutes of Health: Coronavirus Disease 2019 \(COVID-19\) Treatment Guidelines](#) [↗](#). The recommendations in the guidelines were based on scientific evidence and will be updated as more data becomes available.

# Clinical Presentation

## Incubation period

The incubation period for COVID-19 is thought to extend to 14 days, with a median time to symptoms onset.<sup>1-3</sup> One study reported that 97.5% of persons with COVID-19 who developed 11.5 days of SARS-CoV-2 infection.<sup>3</sup>

## Presentation

The signs and symptoms of COVID-19 present at illness onset vary, but over the course of COVID-19 will experience the following<sup>1,4-9</sup>:

- Fever (83–99%)
- Cough (59–82%)
- Fatigue (44–70%)
- Anorexia (40–84%)
- Shortness of breath (31–40%)
- Sputum production (28–33%)
- Myalgias (11–35%)

Atypical presentations have been described, and older adults and persons with medical comorbidities may present with atypical presentations of fever and respiratory symptoms.<sup>10,11</sup> In one study of 1,099 hospitalized patients, 44% had fever at hospital admission but later developed in 89% during hospitalization.<sup>1</sup> Headache, sore throat, hemoptysis, vomiting, and diarrhea have been reported but are less common (<10%).<sup>1</sup> Some COVID-19 patients have experienced gastrointestinal symptoms such as diarrhea and nausea prior to respiratory tract signs and symptoms.<sup>9</sup> Anosmia or ageusia preceding the onset of respiratory symptoms has been anecdotally reported<sup>12</sup>, but more information is needed to understand its role in identifying COVID-19.

Several studies have reported that the signs and symptoms of COVID-19 in children are similar to adults but are generally milder compared to adults.<sup>13-17</sup> For more information on the clinical presentation and course of COVID-19 in children, see [Information for Pediatric Healthcare Providers](#).

## Asymptomatic and Pre-Symptomatic Infection

Several studies have documented SARS-CoV-2 infection in patients who never develop symptoms or patients not yet symptomatic (pre-symptomatic).<sup>14,16,18-28</sup> Since asymptomatic persons are prevalent, the prevalence of asymptomatic infection and detection of pre-symptomatic infection is not well understood. It was found that as many as 13% of RT-PCR-confirmed cases of SARS-CoV-2 infection in children in a study of skilled nursing facility residents infected with SARS-CoV-2 from a healthcare worker were asymptomatic or pre-symptomatic at the time of contact tracing evaluation and testing.<sup>26</sup> Abnormalities on chest imaging before the onset of symptoms.<sup>20,21</sup> Some data suggest that infection tended to be detected in younger individuals and was less likely to be associated with viral

## Asymptomatic and Pre-Symptomatic Transmission

Epidemiologic studies have documented SARS-CoV-2 transmission during the pre-symptomatic and asymptomatic periods, and asymptomatic transmission has been suggested in other reports.<sup>22,23,32</sup> Virologic studies of SARS-CoV-2 with RT-PCR low cycle thresholds, indicating larger quantities of viral RNA, and culture studies have shown asymptomatic and pre-symptomatic SARS-CoV-2 infection.<sup>19,24,26,33</sup> The exact degree of viral shedding that confers risk of transmission is not yet clear. Risk of transmission is thought to be highest in asymptomatic individuals since viral shedding is greatest at the time of symptom onset and declines over days to weeks.<sup>33-36</sup> However, the proportion of SARS-CoV-2 transmission in the population that is asymptomatic compared to symptomatic infection is unclear.<sup>37</sup>

## Clinical Course

### Illness Severity

The largest cohort of >44,000 persons with COVID-19 from China showed that illness severity ranged from mild to critical:<sup>38</sup>

- Mild to moderate (mild symptoms up to mild pneumonia): 81%
- Severe (dyspnea, hypoxia, or >50% lung involvement on imaging): 14%
- Critical (respiratory failure, shock, or multiorgan system dysfunction): 5%

In this study, all deaths occurred among patients with critical illness and the overall case fatality rate among patients with critical disease was 49%.<sup>38</sup> Among children in China, illness severity ranged from asymptomatic, mild or moderate disease, 5% having severe disease, and <1% having critical disease. Among COVID-19 cases with known disposition, the proportion of persons who were hospitalized was 10%, and the proportion of persons with COVID-19 admitted to the intensive care unit (ICU) was 6%.<sup>39</sup>

## Clinical Progression

Among patients who developed severe disease, the median time to dyspnea ranged from 8 to 12 days, and the median time to acute respiratory distress syndrome (ARDS) ranged from 8 to 12 days, and the median time from 10 to 12 days.<sup>5,6,10,11</sup> Clinicians should be aware of the potential for some patients to deteriorate after illness onset. Among all hospitalized patients, a range of 26% to 32% of patients were admitted to the ICU. Among all patients, a range of 3% to 17% developed ARDS compared to a range of 20% to 28% and 67% to 85% for patients admitted to the ICU.<sup>1,4-6,8,11</sup> Mortality among patients admitted to the ICU was 25% to 72% depending on the study.<sup>5,8,10,11</sup> The median length of hospitalization among survivors

## Risk Factors for Severe Illness

Age is a strong risk factor for severe illness, complications, and death.<sup>1,6,8,10,11,38-41</sup> Among reported cases of COVID-19 in China, the case fatality rate was highest among older persons: ≥80 years: 3.6%, 60–69 years: 1.3%, 50–59 years: 0.4%, 40–49 years: 0.4%, <40 years: 0.2%.<sup>38,42</sup> Early U.S. experience with COVID-19 showed that the case fatality was highest in persons aged ≥85 years (range 10%–27%), followed by 3%–11% for ages 75–84 years, 1%–3% for ages 55–64 years, and <1% for ages 0–54 years.<sup>39</sup>

Patients in China with no reported underlying medical conditions had an overall case fatality rate higher for patients with comorbidities: 10.5% for those with cardiovascular disease, 7.3% for those with chronic respiratory disease, hypertension, and cancer.<sup>42</sup> Heart disease, hyperlipidemia, chronic lung disease, and chronic kidney disease have all been associated with increased COVID-19 outcomes.<sup>1,6,10,11,38,42,43</sup> Accounting for differences in age and prevalence of underlying conditions, COVID-19 in the United States was similar to China.<sup>39,40,44</sup>

## Medications

It has been hypothesized that angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor antagonists (ARBs) may increase the risk of SARS-CoV-2 infection and COVID-19 severity.<sup>45</sup> ACE inhibitors and ARBs are part of the renin-angiotensin system (RAS). SARS-CoV-2 uses the ACE2 receptor to enter cells. Recent data to suggest a link between ACE inhibitors or ARBs with worse COVID-19 outcomes. The American Heart Association (AHA), the Heart Failure Society of America (HFSA), and the American College of Cardiology (ACC) are recommending continuation of these drugs for patients already receiving them for heart failure, hypertension, or ischemic heart disease.<sup>46</sup>

It has also been hypothesized that non-steroidal anti-inflammatory drugs (NSAIDs) may worsen COVID-19 outcomes. There are no data suggesting an association between COVID-19 clinical outcomes and NSAID use.

be found at [Healthcare Professionals: Frequently Asked Questions and Answers](#).

## Reinfection

There are no data concerning the possibility of re-infection with SARS-CoV-2 after recovery. Shedding declines with resolution of symptoms, and may continue for days to weeks.<sup>11,33,35</sup> RNA during convalescence does not necessarily indicate the presence of viable infectious virus. Shedding of SARS-CoV-2 RNA is correlated with the detection of IgM and IgG antibodies which signal the development of immunity.

## Viral Testing

Diagnosis of COVID-19 requires detection of SARS-CoV-2 RNA by reverse transcription polymerase chain reaction (RT-PCR). Detection of SARS-CoV-2 viral RNA is better in nasopharynx samples compared to throat swabs. Lower respiratory samples may have better yield than upper respiratory samples.<sup>33,50</sup> SARS-CoV-2 RNA has been detected in stool and blood.<sup>13,34,47,51</sup> Detection of SARS-CoV-2 RNA in blood may be a marker of severe illness. Viral RNA may persist over longer periods among older persons and those who had severe illness (median range of viral shedding among hospitalized patients 12–20 days).<sup>11,33-36</sup>

Infection with both SARS-CoV-2 and with other respiratory viruses has been reported, and detection of another respiratory pathogen does not rule out COVID-19.<sup>53</sup>

For more information about testing and specimen collection, handling and storage, visit [Evidence-Based Diagnostic Testing for Coronavirus Disease 2019 \(COVID-19\)](#) and [Frequently Asked Questions on COVID-19 Testing](#).

## Laboratory and Radiographic Findings

### Laboratory Findings

Lymphopenia is the most common lab finding in COVID-19 and is found in as many as 83% of patients. Lymphopenia, neutrophilia, elevated serum alanine aminotransferase and aspartate aminotransferase, elevated lactate dehydrogenase, high CRP, and high ferritin levels may be associated with greater severity. D-dimer and lymphopenia have been associated with mortality.<sup>8,11</sup> Procalcitonin is typically elevated in COVID-19 and may increase among those admitted to the ICU.<sup>4-6</sup> Patients with critical illness had high proinflammatory cytokine levels, suggesting potential immune dysregulation.<sup>5,55</sup>

### Radiographic Findings

Chest radiographs of patients with COVID-19 typically demonstrate bilateral air-space consolidation. Some patients may have unremarkable chest radiographs early in the disease.<sup>1,5,56</sup> Chest CT images from patients demonstrate bilateral, peripheral ground glass opacities.<sup>4,8,38,56-65</sup> Because this chest CT imaging can overlap with other infections, the diagnostic value of chest CT imaging for COVID-19 is limited upon interpretations from individual radiologists.<sup>57,66</sup> One study found that 56% of patients at the time of diagnosis had a normal CT<sup>58</sup>. Conversely, other studies have also identified chest CT as useful for the detection of SARS-CoV-2 RNA.<sup>56,67</sup> Given the variability in chest imaging findings, chest CT is not recommended for the diagnosis of COVID-19. The American College of Radiology also does not recommend screening or as a first-line test for diagnosis of COVID-19. (See [American College of Radiology](#))

## Clinical Management and Treatment

### Mild to Moderate Disease

Patients with a mild clinical presentation (absence of viral pneumonia and hypoxia) may not require hospitalization, and many patients will be able to manage their illness at home. The decision on inpatient or outpatient setting should be made on a case-by-case basis. This decision will be based on clinical presentation, requirement for supportive care, potential risk factors for severe disease, and ability to self-isolate at home. Patients with risk factors for severe illness (see [People Who Are at High Risk for Severe Illness](#)) should be monitored closely given the possible risk of progression to severe illness in the early stages of onset.<sup>5,6,10,11</sup>

For information regarding infection prevention and control recommendations, please see [Infection Prevention and Control Recommendations for Patients with Confirmed Coronavirus Disease 2019 \(COVID-19\) in Healthcare Settings](#).

### Severe Disease

Some patients with COVID-19 will have severe disease requiring hospitalization for management. There is no specific treatment for COVID-19 that is currently FDA approved. Corticosteroids have been widely used in hospital settings for severe illness in China<sup>6,8,10,11</sup>; however, the benefit of corticosteroid use cannot be determined based on observational data. By contrast, patients with MERS-CoV or influenza who were given corticosteroids have prolonged viral replication, receive mechanical ventilation, and have higher mortality. Corticosteroid use should be avoided unless indicated for other reasons, such as management of chronic obstructive pulmonary disease exacerbation or septic shock. More information can be found at [Healthcare Professionals and Answers](#).

Inpatient management revolves around the supportive management of the most common COVID-19: pneumonia, hypoxemic respiratory failure/ARDS, sepsis and septic shock, cardiac acute kidney injury, and complications from prolonged hospitalization including secondary thromboembolism, gastrointestinal bleeding, and critical illness polyneuropathy/myopathy.

The Infectious Diseases Society of America has released guidelines on the treatment and management of COVID-19. For more information, please visit: [Infectious Diseases Society of America Guideline for the Management of Patients with COVID-19 Infection](#). [↗](#)

The World Health Organization and the Surviving Sepsis Campaign have both released guidance on inpatient management of patients with COVID-19, including those who are critically ill. For more information, see [Guidance on Clinical Management of Severe Acute Respiratory Infection When Novel Coronavirus Suspected](#) [↗](#) (WHO) and [Surviving Sepsis Campaign: Guidelines on the Management of Critical Illness in Patients with Coronavirus Disease 2019 \(COVID-19\)](#) [↗](#).

For more information on the management of children, see [Information for Pediatric Health Care Providers](#) and [Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Related Organ Dysfunction in Children](#) [↗](#).

## Investigational Therapeutics








No FDA-approved drugs have demonstrated safety and efficacy in randomized controlled trials for COVID-19. Use of investigational therapies for treatment of COVID-19 should ideally be done only in randomized controlled trials. Several clinical trials are underway testing multiple drugs against SARS-CoV-2 and/or immunomodulatory effects that may have clinical benefit. For more information, see [Information for Clinicians on Therapeutic Options for COVID-19 Patients](#). For the information on investigational drugs in the U.S., see [ClinicalTrials.gov](#) [↗](#).

## Discontinuation of Transmission-Based Precaution and Isolation

Patients who have clinically recovered and are able to discharge from the hospital but who still require Transmission-Based Precautions may continue isolation at their place of residence. For more information on discontinuation of Transmission-Based Precautions or home isolation of 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](#), [Interim Guidance for Discontinuation of Transmission-Based Precautions and Isolation of Patients with COVID-19](#).

## Patients with COVID-19, and Discontinuation of In-Home Isolation for Immunocompromis

### Additional resources:

- [Information for Pediatric Healthcare Providers](#)
- [Evaluating and Testing Persons for Coronavirus Disease 2019 \(COVID-19\)](#)
- [Frequently Asked Questions on COVID-19 Testing at Laboratories](#)
- [Healthcare Professionals: Frequently Asked Questions and Answers](#)
- [Interim Infection Prevention and Control Recommendations for Patients with Suspec Disease 2019 \(COVID-19\) or in Healthcare Settings](#)
- [World Health Organization. Interim Guidance on Clinical management of severe acut novel coronavirus \(nCoV\) infection is suspected](#) 
- [Surviving Sepsis Campaign: Guidelines on the Management of Critically Ill Adults with \(COVID-19\)](#)  
- [Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and S](#)
- [Surviving Sepsis Campaign International Guidelines for the Management of Septic Sh Organ Dysfunction in Children](#) 
- [Diagnosis and Treatment of Adults with Community-acquired Pneumonia. An Officia the American Thoracic Society and Infectious Diseases Society of America](#) 
- [ACR Recommendations for the use of Chest Radiography and Computed Tomograph Infection](#) 
- [Infectious Diseases Society of America Guidelines on the Treatment and Managemer Infection](#) 
- [National Institutes of Health: Coronavirus Disease 2019 \(COVID-19\) Treatment Guide](#)

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