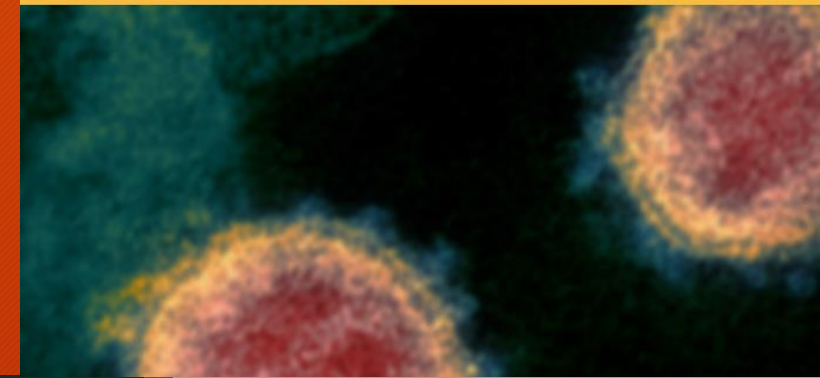


# Coronavirus Disease 2019 (COVID-19)



COVID-19 Treatment Guidelines



COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19)  
Treatment Guidelines. **National Institutes of Health**.

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1

**Dr jafar mohammadshahi**

**Infectious Diseases in Immunocompromised Hosts &  
Transplantation fellowship**

- Individuals of all ages are at risk of SARS-CoV-2 infection.
- people aged  $\geq 65$  years,
- those living in nursing homes or long-term care facilities,
- those who are not vaccinated against COVID-19 or who have poor responses to COVID-19 vaccines
- patients with cardiovascular disease, chronic kidney disease, chronic obstructive pulmonary disease, diabetes with complications, neurocognitive disorders, and obesity are at increased risk of severe COVID-19.
- cancer, cystic fibrosis, immunocompromising conditions, liver disease (especially in patients with cirrhosis), pregnancy, and sickle cell disease.
- Transplant recipients and people who are taking immunosuppressive medications are also at high risk of severe COVID-19.



- vaccination does significantly reduce the risk of COVID-19–related morbidity and mortality, particularly in individuals who are at high risk of progressing to severe disease.

# SARS-CoV-2 Variants

## 4

- Like other RNA viruses, SARS-CoV-2 is constantly evolving through random mutations.
- New mutations can potentially increase or decrease infectiousness and virulence.
- In addition, mutations can increase the virus' ability to evade adaptive immune responses from past SARS-CoV-2 infection or vaccination.
- This viral evolution may increase the risk of reinfection or decrease the efficacy of vaccines.



# SARS-CoV-2 Variants

5

- The Omicron variant was designated in November 2021 and rapidly became the dominant variant across the globe.
- The Omicron subvariants BA.1, BA.1.1, and BA.2 emerged in early to mid-2022, followed by the subvariants BA.4, BA.5, BQ.1, BQ.1.1, and XBB.
- The XBB Omicron subvariant is a recombination of 2 BA.2 subvariants.
- The newer Omicron subvariants are generally more transmissible than previous variants and are not susceptible to any of the anti-SARS-CoV-2 mAbs that were previously authorized for the treatment and prevention of COVID-19.

# SARS-CoV-2 Variants

## 6

- Earlier variants include the Alpha (B.1.1.7) variant, which was first seen in the United Kingdom and shown to be highly infectious; the Beta (B.1.351) variant, which was originally identified in South Africa; the Gamma (P.1) variant, which was identified in Brazil; and the Delta (B.1.617.2) variant, which was identified in India.
- Although the Alpha, Beta, Gamma, and Delta variants were previously designated , they have largely disappeared worldwide.



# Testing for SARS-CoV-2 Infection

7

- The COVID-19 Treatment Guidelines Panel (the Panel) recommends using either a nucleic acid amplification test (NAAT) or an antigen test with a sample collected from the upper respiratory tract (e.g., nasopharyngeal, nasal mid-turbinate, anterior nasal) to diagnose acute SARS-CoV-2 infection (AIII).

# Testing for SARS-CoV-2 Infection

## 8

- A NAAT should not be repeated in an asymptomatic person (with the exception of health care workers) within 90 days of a previous SARS-CoV-2 infection, even if the person has had a significant exposure to SARS-CoV-2.
- SARS-CoV-2 reinfection has been reported in people after an initial diagnosis of the infection; therefore, clinicians should consider using a NAAT for those who have recovered from a previous infection and who present with symptoms that are compatible with SARS-CoV-2 infection if there is no alternative diagnosis (BIII)



# Testing for SARS-CoV-2 Infection

9

- The Panel recommends against diagnosing acute SARS-CoV-2 infection solely on the basis of serologic (i.e., antibody) test results (AIII).

## Prevention of SARS-CoV-2 Infection

- ❖ In poorly ventilated, enclosed spaces, SARS-CoV-2 infection via airborne transmission of small particles can occur after prolonged exposure (i.e., >15 minutes) to a person who is infectious.
- ❖ The risk of SARS-CoV-2 transmission can be reduced by covering coughs and sneezes and maintaining a distance of at least 6 feet from others.
- ❖ Frequent handwashing also effectively reduces the risk of infection.



# Prevention of SARS-CoV-2 Infection

- Transmission of SARS-CoV-2 occurs primarily through exposure to respiratory droplets.
- Exposure can occur when individuals inhale droplets or particles that contain the virus (with the greatest risk of transmission occurring within 6 feet of an infectious source) or touch mucous membranes with hands that have been contaminated with the virus.
- Less commonly, airborne transmission of droplets and particles of SARS-CoV-2 may occur among people who are more than 6 feet apart

# COVID-19 Vaccines

- Vaccination is the most effective way to prevent COVID-19.
- The COVID-19 Treatment Guidelines Panel (the Panel) recommends COVID-19 vaccination for everyone who is eligible according to the CDC's Advisory Committee on Immunization Practices (AI).
- COVID-19 vaccination is recommended for everyone aged  $\geq 6$  months.
- The type and dose of vaccine and the timing of the doses depend on the recipient's age and underlying medical conditions.



# COVID-19 Vaccines

- COVID-19 vaccines are safe and effective.
- Local and systemic adverse events are relatively common with these vaccines.
- There have been a few reports of severe allergic reactions following COVID-19 vaccination, including rare reports of patients who experienced anaphylaxis after receiving an mRNA vaccine.
- Thrombosis with thrombocytopenia syndrome is a serious condition characterized by blood clots in large blood vessels and low platelet levels.
- Myocarditis and pericarditis after COVID-19 vaccination are rare, and most of the reported cases were very mild and self-limiting.

# Clinical Spectrum of SARS-CoV-2 Infection

14

- Patients with SARS-CoV-2 infection can experience a range of clinical manifestations, from no symptoms to critical illness.
- In general, adults with SARS-CoV-2 infection can be grouped into the following severity of illness categories:
  - ✓ Asymptomatic or presymptomatic infection
  - ✓ Mild illness
  - ✓ Moderate illness
  - ✓ Severe illness
  - ✓ Critical illness



# Clinical Spectrum of SARS-CoV-2 Infection

15

- Asymptomatic or presymptomatic infection: Individuals who test positive for SARS-CoV-2 using a virologic test (i.e., a nucleic acid amplification test [NAAT] or an antigen test) but have no symptoms consistent with COVID-19.
- Mild illness: Individuals who have any of the various signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but do not have shortness of breath, dyspnea, or abnormal chest imaging.

# Clinical Spectrum of SARS-CoV-2 Infection

16

- Moderate illness: Individuals who show evidence of lower respiratory disease during clinical assessment or imaging and who have an oxygen saturation measured by pulse oximetry (SpO<sub>2</sub>)  $\geq 94\%$  on room air at sea level.
- Severe illness: Individuals who have SpO<sub>2</sub>  $< 94\%$  on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO<sub>2</sub>/FiO<sub>2</sub>)  $< 300$  mm Hg, a respiratory rate  $> 30$  breaths/min, or lung infiltrates  $> 50\%$ .
- Critical illness: Individuals who have respiratory failure, septic shock, and/or multiple organ dysfunction.



# Clinical Spectrum of SARS-CoV-2 Infection

17

- The initial evaluation for patients may include chest imaging (e.g., X-ray, ultrasound or computed tomography scan) and an electrocardiogram.
- Laboratory testing should include a complete blood count with differential and a metabolic profile, including liver and renal function tests.
- Although inflammatory markers such as C-reactive protein (CRP), D-dimer, and ferritin are not routinely measured as part of standard care, results from such measurements may have prognostic value.

- infectious complications in patients with COVID-19 can be categorized as follows:
  - • Coinfections at presentation
  - • Reactivation of latent infections
  - • Nosocomial infections
  - • Opportunistic fungal infections



- **Coinfections at presentation :**

- Although most individuals present with only SARS-CoV-2 infection, concomitant viral infections, including influenza and other respiratory viruses, have been reported.
- Community-acquired bacterial pneumonia has also been reported, but it is uncommon, with a prevalence that ranges from 0% to 6% of people with SARS-CoV-2 infection.
- Antibacterial therapy is generally not recommended unless additional evidence for bacterial pneumonia is present (e.g., leukocytosis, the presence of a focal infiltrate on imaging).

- Reactivation of latent infections :

- There are case reports of underlying chronic hepatitis B virus and latent tuberculosis infections reactivating in patients with COVID-19 who receive immunomodulators as treatment, although the data are currently limited.
- Reactivation of herpes simplex virus and varicella zoster virus infections have also been reported.
- Cases of severe and disseminated strongyloidiasis have been reported in patients with COVID-19 during treatment with tocilizumab and corticosteroids.



- **Nosocomial infection :**

- Hospitalized patients with COVID-19 may acquire common nosocomial infections, such as hospital-acquired pneumonia (including ventilator-associated pneumonia), line-related bacteremia or fungemia, catheter-associated urinary tract infection, and Clostridioides difficile–associated diarrhea.
- Early diagnosis and treatment of these infections are important for improving outcomes in these patients.

- Opportunistic fungal infections:

- Invasive fungal infections, including aspergillosis and mucormycosis, have been reported in hospitalized patients with COVID-19.
- Although these infections are relatively rare, they can be fatal, and they may be seen more commonly in patients who are immunocompromised or receiving mechanical ventilation.
- The majority of mucormycosis cases have been reported in India and are associated with diabetes mellitus or the use of corticosteroids.
- The approach for managing these fungal infections should be the same as the approach for managing invasive fungal infections in other settings.



# SARS-CoV-2 Reinfection and Breakthrough Infection

23

- As seen with other respiratory viral infections, reinfection after recovery from prior infection has been reported for SARS-CoV-2.
  - Reinfection may occur as initial immune responses to the primary infection wane over time.
- 
- Breakthrough SARS-CoV-2 infections (i.e., infection in people who completed the primary vaccine series with or without booster doses) also occurs.
  - When compared with infection in people who are unvaccinated, breakthrough infection appears less likely to lead to severe illness or symptoms that persist  $\geq 28$  days.

# SARS-CoV-2 Reinfection and Breakthrough Infection

24

- Breakthrough SARS-CoV-2 infections (i.e., infection in people who completed the primary vaccine series with or without booster doses) also occurs.
- When compared with infection in people who are unvaccinated, breakthrough infection appears less likely to lead to severe illness or symptoms that persist  $\geq 28$  days.
- The time to breakthrough infection has been reported to be shorter for patients with immunocompromising conditions (i.e., solid organ or bone marrow transplant recipients or people with HIV) than for those with no immunocompromising conditions.



# Clinical Management of Adults

25

- Two main processes are thought to drive the pathogenesis of COVID-19.
- Early in the clinical course, the disease is primarily driven by the replication of SARS-CoV-2.
- Later in the clinical course, the disease appears to be driven by a dysregulated immune/inflammatory response to SARS-CoV-2 that leads to tissue damage.
- Based on this understanding, therapies that directly target SARS-CoV-2 are anticipated to have the greatest effect early in the course of the disease, while immunosuppressive/anti-inflammatory therapies are likely to be more beneficial in the later stages of COVID-19.

## General Management of Nonhospitalized Adults With Acute COVID-19

26

- Management of nonhospitalized patients with acute COVID-19 should include providing supportive care, taking steps to reduce the risk of SARS-CoV-2 transmission (including isolating the patient), and advising patients on when to contact a health care provider and seek an in-person evaluation (AIII).
- Patients who are at high risk of progression to severe COVID-19 may be eligible for pharmacologic therapy.
- Patients with persistent or progressive dyspnea, especially those who have an oxygen saturation measured by pulse oximetry ( $\text{SpO}_2$ )  $\leq 94\%$  on room air at sea level or have symptoms that suggest high acuity (e.g., chest pain or tightness, dizziness, confusion, other mental status changes), should be referred to a health care provider for an in-person evaluation (AIII).



**Table 2a. Therapeutic Management of Nonhospitalized Adults With Mild to Moderate COVID-19 Who Do Not Require Supplemental Oxygen**

Patient Disposition	Panel's Recommendations
All Patients	<ul style="list-style-type: none"> <li>• Symptom management should be initiated for all patients <b>(AIII)</b>.</li> <li>• The Panel <b>recommends against</b> the use of <b>dexamethasone<sup>a</sup></b> or other systemic corticosteroids in the absence of another indication <b>(AIIb)</b>.</li> </ul>
Patients Who Are at High Risk of Progressing to Severe COVID-19 <sup>b,c</sup>	<p><i>Preferred therapies. Listed in order of preference:</i></p> <ul style="list-style-type: none"> <li>• <b>Ritonavir-boosted nirmatrelvir (Paxlovid)<sup>d</sup> (AIIa)</b>; see footnote on drug interactions<sup>e</sup></li> <li>• <b>Remdesivir<sup>d,f</sup> (BIIa)</b></li> </ul> <p><i>Alternative therapy. For use when the preferred therapies are not available, feasible to use, or clinically appropriate:</i></p> <ul style="list-style-type: none"> <li>• <b>Molnupiravir<sup>d,g,h</sup> (CIIa)</b></li> </ul>
<p>Each recommendation in the Guidelines receives a rating for the strength of the recommendation (A, B, or C) and a rating for the evidence that supports it (I, IIa, IIb, or III). See <a href="#">Guidelines Development</a> for more information.</p>	

**Table 2a. Therapeutic Management of Nonhospitalized Adults With Mild to Moderate COVID-19 Who Do Not Require Supplemental Oxygen**

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- There is currently a lack of safety and efficacy data on the use of dexamethasone in outpatients with COVID-19.
- Using systemic glucocorticoids in outpatients with COVID-19 may cause harm.



**Table 2a. Therapeutic Management of Nonhospitalized Adults With Mild to Moderate COVID-19 Who Do Not Require Supplemental Oxygen**

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Each recommendation in the Guidelines receives a rating for the strength of the recommendation (A, B, or C) and a rating for the evidence that supports it (I, IIa, IIb, or III). See <a href="#">Guidelines Development</a> for more information.	

# Therapeutic Management of Hospitalized Adults With COVID-19

30

**Table 2b. Therapeutic Management of Hospitalized Adults With COVID-19**

Disease Severity	Recommendations for Antiviral or Immunomodulator Therapy		Recommendations for Anticoagulant Therapy
	Clinical Scenario	Recommendation	
Hospitalized for Reasons Other Than COVID-19	Patients with mild to moderate COVID-19 who are at high risk of progressing to severe COVID-19 <sup>a,b</sup>	See <a href="#">Therapeutic Management of Nonhospitalized Adults With COVID-19</a> .	For patients without an indication for therapeutic anticoagulation: <ul style="list-style-type: none"> <li>• <b>Prophylactic dose of heparin</b>, unless contraindicated (AI); (BIII) for pregnant patients</li> </ul>
Hospitalized but Does Not Require Supplemental Oxygen	All patients	The Panel <b>recommends against</b> the use of <b>dexamethasone (AIIa)</b> or other systemic corticosteroids (AIII) for the treatment of COVID-19. <sup>c</sup>	
	Patients who are at high risk of progressing to severe COVID-19 <sup>a,b</sup>	<b>Remdesivir<sup>d</sup> (BIIb)</b> for patients who are immunocompromised; (BIII) for other high-risk patients	
Hospitalized and Requires Conventional Oxygen*	Patients who require minimal conventional oxygen	<b>Remdesivir<sup>d,f</sup> (BIIa)</b>	For nonpregnant patients with D-dimer levels above the ULN who do not have an increased bleeding risk: <ul style="list-style-type: none"> <li>• <b>Therapeutic dose of heparin<sup>h</sup> (CIIa)</b></li> </ul>
	Most patients	Use <b>dexamethasone plus remdesivir<sup>f</sup> (BIIa)</b> . If remdesivir cannot be obtained, use <b>dexamethasone (BI)</b> .	
	Patients who are receiving dexamethasone and who have rapidly increasing oxygen needs and systemic inflammation	Add 1 of the following immunomodulators: <sup>g</sup> <i>Preferred</i> <ul style="list-style-type: none"> <li>• <b>PO baricitinib (BIIa)</b></li> <li>• <b>IV tocilizumab (BIIa)</b></li> </ul> <i>Alternatives</i> <ul style="list-style-type: none"> <li>• <b>IV abatacept (CIIa)</b></li> <li>• <b>IV infliximab (CIIa)</b></li> </ul>	For other patients: <ul style="list-style-type: none"> <li>• <b>Prophylactic dose of heparin</b>, unless contraindicated (AI); (BIII) for pregnant patients</li> </ul>



# Therapeutic Management of Hospitalized Adults With COVID-19

31

Disease Severity	Recommendations for Antiviral or Immunomodulator Therapy		Recommendations for Anticoagulant Therapy
	Clinical Scenario	Recommendation	
Hospitalized and Requires HFNC Oxygen or NIV	All patients	<p><b>Dexamethasone</b> should be administered to all patients (AI). If not already initiated, promptly add 1 of the following immunomodulators:</p> <p><i>Preferred</i></p> <ul style="list-style-type: none"> <li>• PO baricitinib<sup>g,i</sup> (AI)</li> </ul> <p><i>Preferred Alternative</i></p> <ul style="list-style-type: none"> <li>• IV tocilizumab<sup>g,i</sup> (BIIa)</li> </ul> <p><i>Additional Alternatives (Listed in Alphabetical Order)</i></p> <ul style="list-style-type: none"> <li>• IV abatacept<sup>g,i</sup> (CIIa)</li> <li>• IV infliximab<sup>g,i</sup> (CIIa)</li> </ul> <p>Add remdesivir to 1 of the options above in certain patients (for examples, see footnote).<sup>i</sup></p>	<p>For patients without an indication for therapeutic anticoagulation:</p> <ul style="list-style-type: none"> <li>• <b>Prophylactic dose of heparin</b>, unless contraindicated (AI); (BIII) for pregnant patients</li> </ul> <p>For patients who are started on a therapeutic dose of heparin in a non-ICU setting and then transferred to the ICU, the Panel recommends switching to a <b>prophylactic dose of heparin</b>, unless there is another indication for therapeutic anticoagulation (BIII).</p>
Hospitalized and Requires MV or ECMO	All patients	<p><b>Dexamethasone</b> should be administered to all patients (AI). If the patient has not already received a second immunomodulator, promptly add 1 of the following (listed in alphabetical order):</p> <ul style="list-style-type: none"> <li>• PO baricitinib<sup>i,k</sup> (BIIa)</li> <li>• IV tocilizumab<sup>i,k</sup> (BIIa)</li> </ul>	

# Therapeutic Management of Hospitalized Adults With COVID-19

32

- Contraindications for the use of therapeutic anticoagulation in patients with COVID-19 include a **PLT <50 x 10<sup>9</sup>/L**, Hgb <8 g/dL, **the need for dual antiplatelet therapy**, bleeding within the past 30 days that required an ED visit or hospitalization, **a history of a bleeding disorder**, or an inherited or active acquired bleeding disorder.



# Therapeutic Management of Hospitalized Adults With COVID-19

33

- ECMO = extracorporeal membrane oxygenation;
- ED = emergency department;
- HFNC = high-flow nasal cannula;
- JAK = Janus kinase;
- NIV = noninvasive ventilation

Drug Name	Dosing Regimen	Comments
<b>Dexamethasone</b>	DEX 6 mg IV or PO once daily for up to 10 days or until hospital discharge (whichever comes first)	<ul style="list-style-type: none"> <li>• If DEX is not available, an equivalent dose of another corticosteroid may be used.</li> <li>• For more information, see <a href="#">Systemic Corticosteroids</a>.</li> </ul>
<b>Infliximab</b>	Infliximab 5 mg/kg actual body weight administered as a single IV dose	<ul style="list-style-type: none"> <li>• No adjustment based on eGFR</li> </ul>
<b>Heparin</b>	Therapeutic dose of SUBQ LMWH or IV UFH	<ul style="list-style-type: none"> <li>• Administer for 14 days or until hospital discharge (whichever comes first) unless there is a diagnosis of VTE or another indication for therapeutic anticoagulation.</li> </ul>
	Prophylactic dose of SUBQ LMWH or SUBQ UFH	<ul style="list-style-type: none"> <li>• Administer for the duration of the hospital stay.</li> </ul>
<b>Remdesivir</b>	RDV 200 mg IV once, then RDV 100 mg IV once daily for 4 days or until hospital discharge (whichever comes first)	<ul style="list-style-type: none"> <li>• If the patient is hospitalized for reasons other than COVID-19, the treatment duration is 3 days. For more information, see <a href="#">Therapeutic Management of Nonhospitalized Adults With COVID-19</a>.</li> </ul>
<b>Tocilizumab</b>	Tocilizumab 8 mg/kg actual body weight (up to 800 mg) administered as a single IV dose	<ul style="list-style-type: none"> <li>• In clinical trials, a third of the participants received a second dose of tocilizumab 8 hours after the first dose if no clinical improvement was observed.</li> </ul>
<b>Tofacitinib</b>	Tofacitinib 10 mg PO twice daily for up to 14 days or until hospital discharge (whichever comes first)	<ul style="list-style-type: none"> <li>• eGFR &lt;60 mL/min/1.73 m<sup>2</sup>: tofacitinib 5 mg PO twice daily</li> </ul>



# Care of Critically Ill Adults With COVID-19

## Hemodynamics

- For adults with COVID-19 and shock, the COVID-19 Treatment Guidelines Panel (the Panel) recommends using dynamic parameters, skin temperature, capillary refilling time, and/or lactate levels over static parameters to assess fluid responsiveness (**BIIa**).
- For the acute resuscitation of adults with COVID-19 and shock, the Panel recommends using buffered/balanced crystalloids over unbalanced crystalloids (**BIIa**).
- For the acute resuscitation of adults with COVID-19 and shock, the Panel **recommends against** the initial use of **albumin** for resuscitation (**BI**).
- For adults with COVID-19 and shock, the Panel recommends **norepinephrine** as the first-choice vasopressor (**AI**).
- For adults with COVID-19 and shock, the Panel recommends titrating vasoactive agents to target a mean arterial pressure (MAP) of 60 to 65 mm Hg, over higher MAP targets (**BI**).
- The Panel **recommends against** using hydroxyethyl starches for intravascular volume replacement in adult patients with COVID-19 and sepsis or septic shock (**AI**).
- When norepinephrine is available, the Panel **recommends against** using **dopamine** for adult patients with COVID-19 and shock (**AI**).
- As a second-line vasopressor, the Panel recommends adding either **vasopressin** (up to 0.03 units/min) (**BIIa**) or **epinephrine** (**BIIB**) to norepinephrine to raise MAP to target or adding **vasopressin** (up to 0.03 units/min) (**BIIa**) to decrease norepinephrine dosage.
- The Panel **recommends against** using **low-dose dopamine** for renal protection (**AI**).
- The Panel recommends using **dobutamine** in adult patients with COVID-19 who show evidence of cardiac dysfunction and persistent hypoperfusion despite adequate fluid loading and the use of vasopressor agents (**BIII**).
- The Panel recommends that all adult patients with COVID-19 who require vasopressors have an arterial catheter placed as soon as practical, if resources are available (**BIII**).
- For adult patients with refractory septic shock who have completed a course of corticosteroids to treat COVID-19, the Panel recommends using low-dose corticosteroid therapy (“shock-reversal”) over no corticosteroid therapy (**BIIa**).



## Oxygenation and Ventilation

- For adults with COVID-19 and acute hypoxemic respiratory failure despite conventional oxygen therapy, the Panel recommends starting therapy with high-flow nasal cannula (HFNC) oxygen; if patients fail to respond, noninvasive ventilation (NIV) or intubation and mechanical ventilation should be initiated **(BIIa)**.
- For adults with COVID-19 and acute hypoxemic respiratory failure despite conventional oxygen therapy who do not have an indication for endotracheal intubation and for whom HFNC oxygen is not available, the Panel recommends performing a closely monitored trial of NIV **(BIIa)**.
- For adults with persistent hypoxemia who require HFNC oxygen and for whom endotracheal intubation is not indicated, the Panel recommends a trial of awake prone positioning **(BIIa)**.
- The Panel **recommends against** the use of awake prone positioning as a rescue therapy for refractory hypoxemia to avoid intubation in patients who otherwise meet the indications for intubation and mechanical ventilation **(AIII)**.
- If intubation becomes necessary, the procedure should be performed by an experienced practitioner in a controlled setting due to the enhanced risk of exposing health care practitioners to SARS-CoV-2 during intubation **(AIII)**.
- For mechanically ventilated adults with COVID-19 and acute respiratory distress syndrome (ARDS):
  - The Panel recommends using low tidal volume (VT) ventilation (VT 4–8 mL/kg of predicted body weight) over higher VT ventilation (VT >8 mL/kg) **(AI)**.
  - The Panel recommends targeting plateau pressures of <30 cm H<sub>2</sub>O **(AIIa)**.

- The Panel recommends using a conservative fluid strategy over a liberal fluid strategy (**BIIa**).
- The Panel **recommends against** the routine use of inhaled nitric oxide (**AIIa**).
- For mechanically ventilated adults with COVID-19 and moderate to severe ARDS:
  - The Panel recommends using a higher positive end-expiratory pressure (PEEP) strategy over a lower PEEP strategy (**BIIa**).
  - For mechanically ventilated adults with COVID-19 and refractory hypoxemia despite optimized ventilation, the Panel recommends prone ventilation for 12 to 16 hours per day over no prone ventilation (**BIIa**).
  - The Panel recommends using, as needed, intermittent boluses of neuromuscular blocking agents (NMBAs) or a continuous NMBA infusion to facilitate protective lung ventilation (**BIIa**).
- For mechanically ventilated adults with COVID-19, severe ARDS, and hypoxemia despite optimized ventilation and other rescue strategies:
  - The Panel recommends using recruitment maneuvers rather than not using recruitment maneuvers (**CIIa**).
  - If recruitment maneuvers are used, the Panel **recommends against** the use of staircase (incremental PEEP) recruitment maneuvers (**AIIa**).
  - The Panel recommends using an inhaled pulmonary vasodilator as a rescue therapy; if no rapid improvement in oxygenation is observed, the treatment should be tapered off (**CIII**).

### Pharmacologic Interventions

- In the absence of a proven or suspected bacterial infection, the Panel **recommends against** the use of empiric broad-spectrum antibiotics in adult patients with severe or critical COVID-19 (**BIII**).
- As with any hospitalized patient, adult patients with COVID-19 who receive antibiotics should be reassessed daily to minimize the adverse consequences of unnecessary antimicrobial therapy (**AIII**).

### Extracorporeal Membrane Oxygenation

- There is insufficient evidence for the Panel to recommend either for or against the use of extracorporeal membrane oxygenation in adults with COVID-19 and refractory hypoxemia.





**TANK YOU**