

GUIDELINES FOR THE CARE OF ADULT PATIENTS WITH SEVERE OR CRITICAL COVID-19 IN THE AMERICAS

Abridged version, 4th edition

PAHO



Pan American
Health
Organization



World Health
Organization
REGIONAL OFFICE FOR THE
Americas

NOTE ON THIS EDITION

These guidelines are the result of a rapid development process. The information included in this document reflects the evidence as of the date of publication. The information and recommendations are based on the GRADE approach to the available evidence and its certainty at the date of publication. However, in light of the numerous ongoing studies, the Pan American Health Organization will regularly update the evidence and corresponding recommendations.

Updated November 2022



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PAHO/IMS/EIH/COVID-19/22-0038

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OBJECTIVES AND TARGET POPULATION

These clinical practice guidelines were developed to provide recommendations for the prophylaxis and management of patients with non-severe coronavirus disease 2019 (COVID-19), as well as individuals at risk of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in Latin America and the Caribbean.

The target population consists of people at risk of SARS-CoV-2 infection, patients with a presumptive or confirmed COVID-19 diagnosis, and patients with non-severe COVID-19. According to the World Health Organization (WHO), it is important to identify the stages of severity of SARS-CoV-2 infection, which are defined in Table 1.

Table 1. World Health Organization definitions of COVID-19 severity

Critical COVID-19: Defined by the criteria for acute respiratory distress syndrome, sepsis, septic shock, or other conditions that normally require the provision of life-sustaining therapies such as mechanical ventilation (invasive or non-invasive) or vasopressor therapy.

• **Severe COVID-19:** Defined by any of the following signs:

- oxygen saturation <90% on room air;
- respiratory rate >30 breaths per minute (bpm) in adults and children >5 years of age, ≥60 bpm in children <2 months, ≥50 bpm in children 2 to 11 months, and ≥40 rpm in children 1 to 5 years; or signs of severe respiratory distress (accessory muscle use, inability to complete full sentences, and, in children, very severe chest wall indrawing, grunting, central cyanosis, or presence of any other general danger signs).

• **Non-severe COVID-19:** Defined as absence of any criteria for severe or critical COVID-19.

Caution: The WHO panel of experts notes that the oxygen saturation threshold of 90% to define severe COVID-19 is arbitrary and should be interpreted cautiously. For example, clinicians must use their judgment to determine whether a low oxygen saturation is a sign of severity or is normal for a given patient with chronic lung disease. Similarly, >90–94% saturation on room air is abnormal (in patients with healthy lungs) and can be an early sign of severe disease, if the patient is on a downward trend. Generally, if there is any doubt, the panel suggested it is preferable to consider the illness as severe.

Source: World Health Organization. COVID-19 clinical management: living guidance, 25 January 2021. Geneva: WHO; 2021. Available from: <https://www.who.int/en/publications/i/item/WHO-2019-nCoV-clinical-2021-1>.

SCOPE AND USERS

These clinical practice guidelines provide evidence-informed recommendations for identifying markers and mortality risk factors in critically ill patients, as well as infection control, sample collection, supportive care (respiratory and hemodynamic), pharmacological treatment, early rehabilitation, diagnostic imaging use, prevention of complications, and discharge requirements.

The recommendations are for all healthcare staff who deal with patients in emergency departments and ICUs (physicians specializing in emergency medicine, pulmonology, intensive care medicine, internal medicine, anesthesiology, and infectious diseases; respiratory therapists, physical therapists, nurses, and pharmaceutical chemists). These guidelines are intended for use by decision-makers and government entities involved in the management of patients with COVID-19 in ICUs in the Region of the Americas.

These guidelines do not address matters related to nutrition or management of complications.

METHODOLOGY

These guidelines follow the GRADE methodology (Grading of recommendations assessment, development, and evaluation) for the rapid development of the guidelines proposed by the Pan American Health Organization (PAHO) and WHO.

A multidisciplinary development group was formed by experts in critical care medicine, emergency medicine, infectious disease, anesthesiology, pediatrics, pulmonology, epidemiology, and public health. Experts from the Pan American Health Organization were responsible for technical and methodological coordination. A prioritization process was done in order to select the questions that needed to be updated and the new questions that were included in this version of the guideline. A systematic search of the literature was completed. After the evidence selection process was conducted, the GRADE evidence profiles were created. A virtual panel of Ibero-American experts was subsequently convened to formulate recommendations, considering the context for regional implementation. All members of the development group signed conflict of interest forms, which were reviewed by the guideline coordinators. Details of the methodology are found in the long version of the guideline.

CONTINUOUS UPDATING OF GUIDELINES

These guidelines undergo a continuous process of updating evidence (live guide) in order to provide the most current recommendations for management of critically ill patients with COVID-19. Particular attention was given to potential pharmacological treatments, such as the use of antivirals, immunomodulators, tocilizumab, ivermectin, convalescent plasma, and antibiotics, among others.

SUMMARY OF THE RECOMMENDATIONS


How to use these guidelines


For each clinical question, a set of recommendations and good practices provides guidance for the management of critically ill patients with COVID-19.


Each recommendation shows the certainty of the evidence according to the GRADE system:


CERTAINTY	CHARACTERISTICS
● ● ● ● High	Further research is very unlikely to change our confidence in the estimate of effect.
● ● ● ○ Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
● ● ○ ○ Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
● ○ ○ ○ Very low	Any estimate of effect is very uncertain.


The recommendations also indicate the strength of the recommendation according to the GRADE system:

- 

Should be used. New evidence is unlikely to change the recommendation.
Recommended
- 

Could be used. New evidence may change the recommendation.
Suggested
- 

Should not be used. New evidence may change the recommendation.
Not suggested
- 

Should not be used. New evidence may change the recommendation.
Not recommended
- 

Good practice statement

Key recommendations for implementation of the guidelines are identified by an asterisk (*).

SUMMARY OF RECOMMENDATIONS FOR THE MANAGEMENT OF CRITICALLY ILL ADULTS PATIENTS WITH COVID-19

These recommendations are subject to review as new evidence becomes available.

QUESTION 1.

WHAT ARE THE FACTORS AND MARKERS THAT PREDICT MORTALITY AND DISEASE PROGRESSION IN CRITICALLY ILL PATIENTS WITH COVID-19?


*Updated question

N.º	RECOMENDATION
1	<p>For the clinical management of adult and pediatric patients with severe or critical COVID-19 (including pregnant women), it is recommended to consider at least one of the following risk factors for disease progression: older adult, presence of more than one comorbidity (hypertension, obesity, diabetes, cardiovascular disease, chronic lung disease, chronic kidney disease, chronic liver disease, cerebrovascular disease, thrombocytopenia, active smoker, malnutrition in geriatric patients, cancer, unvaccinated, patients with transplants, and diseases that cause immunodeficiency).</p> <p>Strong recommendation. Certainty of the evidence: moderate and low</p>
2	<p>It is suggested to monitor, according to availability and clinical criteria, the following markers that have been associated with increased mortality in critically ill patients with COVID-19: elevated leukocyte count, lactic dehydrogenase, C-reactive protein, ferritin fibrinogen, creatinine, urea, cardiac troponin, and D-dimer, as well as markers related to secondary infections such as decreased albumin levels and low platelet count. If available, monitoring for interleukin-6 is also suggested.</p> <p>Conditional recommendation. Certainty of the evidence: moderate and low</p>
✓	<p>Critically ill patients with COVID-19 should be monitored for signs and symptoms suggesting venous or arterial thromboembolism (such as infarction), deep vein thrombosis, pulmonary embolism, or acute coronary syndrome. Proceed according to institutional protocols.</p> <p>Good practice statement</p>

QUESTION 2.

WHAT TRIAGE STRATEGY SHOULD BE USED FOR CRITICALLY ILL PATIENTS WITH COVID-19?


*Updated question







N.º	RECOMENDATION
	<p>Institutional protocols for triage of patients with a suspected or confirmed diagnosis of COVID-19 should be implemented in order to appropriately classify patients who require management in an intensive care unit.</p> <p>Duration and severity of symptoms, findings of diagnostic imaging (radiography, computed tomography, or lung ultrasound), origin of pulmonary infiltrates, oxygenation needs, vital organ dysfunction, sepsis, and septic shock should be evaluated to identify critically ill patients with COVID-19.</p> <p>The Pan American Health Organization (PAHO) has an algorithm for the management of patients with suspected COVID-19 infection at the first level of care and in remote areas of the Region of the Americas: https://iris.paho.org/handle/10665.2/52501https://iris.paho.org/bitstream/handle/10665.2/56294/OPSIMSEIHCOVID19220020_spa.pdf?sequence=1&isAllowed=y</p> <p>Good practice statement</p>

QUESTION 3.

HOW SAFE AND EFFECTIVE ARE INTERVENTIONS TO PREVENT INFECTION OF HEALTH PROFESSIONALS WHO CARE FOR PATIENTS WITH COVID-19?

*Updated question



N.º	RECOMENDATION
	<p>For health care workers in contact with patients with COVID-19 who perform aerosol-generating* procedures in intensive care units (ICUs) or who work in a unit in which such procedures are performed without adequate ventilation or an independent negative pressure system, it is recommended that medical respirator-type masks (N-95 respirator masks, FFP2, or equivalent) be used, as opposed to surgical masks, in addition to other personal protective equipment (gloves, gown, and eye protection such as a face shield or safety goggles).</p> <p><i>* Aerosol-generating procedures in the ICU include: endotracheal intubation, bronchoscopy, open suctioning, nebulized treatment, manual ventilation before endotracheal intubation, physical proning of the patient, disconnecting the patient from the ventilator, non-invasive positive pressure ventilation, tracheostomy, and cardiopulmonary resuscitation.</i></p> <p>Good practice statement</p>

N.º	RECOMENDATION
	<p>Aerosol-generating procedures performed on patients with COVID-19 in the ICU should be carried out in areas designated for that purpose and the best available measures for limiting contamination of other patients or health care workers should be implemented. If a negative pressure room is not available, an area with natural ventilation should be designated in all patient care areas.</p> <p>Good practice statement</p>
	<p>For natural ventilation, the following minimum hourly averaged ventilation rates are recommended:</p> <ul style="list-style-type: none"> • 160 L/s/patient (hourly average ventilation rate) for airborne precaution rooms (with a minimum of 80 L/s/patient) • When patient care is undertaken in corridors during emergency or other situations, the same ventilation rate requirements for airborne precaution rooms apply. • When natural ventilation alone cannot satisfy the recommended ventilation requirements, alternative ventilation systems, such as hybrid (mixed-mode) natural ventilation should be considered. If that is not enough, mechanical ventilation should be used. <p>Good practice statement</p>
	<p>For health care workers providing care to non-mechanically ventilated COVID-19 patients in the ICU, it is suggested that surgical masks be used rather than respirator masks, in addition to other personal protective equipment.</p> <p>Conditional recommendation. Certainty of the evidence: low</p>
	<p>For health care workers performing non-aerosol-generating procedures on mechanically ventilated (closed-circuit) patients with COVID-19, it is suggested that surgical masks be used rather than respirator masks, in addition to other personal protective equipment.</p> <p>Conditional recommendation. Certainty of the evidence: low</p>
	<p>For health care workers performing endotracheal intubation on patients with COVID-19, it is suggested to use video-guided laryngoscopy, if available, rather than direct laryngoscopy.</p> <p>Conditional recommendation. Certainty of the evidence: low</p>
	<p>For health care workers performing endotracheal intubation on COVID-19 patients, intubation should be performed by the health professional most experienced with airway management, following institutional protocols to minimize the number of attempts and the risk of transmission.</p> <p>Good practice statement</p>

QUESTION 4.

HOW SHOULD SPECIMENS BE COLLECTED FOR THE DIAGNOSIS OF COVID-19 IN PATIENTS REQUIRING INTUBATION AND MECHANICAL VENTILATION?


*Updated question

N.º	RECOMENDATION
<p>6</p>	<p>For adult patients with suspicion of COVID-19 that need to be intubated and mechanically ventilated, it is suggested:</p> <ul style="list-style-type: none"> • For diagnostic testing, samples should be obtained from the lower respiratory tracts (at the time of intubating or as close as possible), rather than obtaining samples from the upper respiratory tract (nasopharyngeal or oropharyngeal samples). • For lower respiratory samples, endotracheal aspirates should be obtained, rather than bronchial wash or bronchoalveolar lavage samples. <p>Conditional recommendation. Certainty of the evidence: low</p>
<p></p>	<p>Rapid collection and testing of specimens from patients with suspected COVID-19 should be a priority and should be carried out by experts in accordance with biosafety recommendations. It is recommended that the laboratory procedure for endotracheal aspirates be institutionally validated in order to avoid false negatives.</p> <p>Additional testing should be conducted in accordance with the need to confirm SARS-CoV-2 and possible coinfections. Institutional guidelines for obtaining informed consent for specimen collection, testing, and future research should be followed.</p> <p>Good practice statement</p>
<p></p>	<p>Tests should be performed for differential diagnosis with other pathologies (e.g. influenza, malaria, dengue) according to clinical features and local epidemiology.</p> <p>Good practice statement</p>

QUESTION 5.



HOW SAFE AND EFFECTIVE ARE INTERVENTIONS FOR RESPIRATORY SUPPORT OF CRITICALLY ILL PATIENTS WITH COVID-19?

*Updated question

N.º	RECOMENDATION
<p></p>	<p>Progression to acute hypoxemic respiratory failure should be promptly recognized when a patient with respiratory distress fails to respond to standard oxygen therapy, and advanced ventilatory support should be provided.</p> <p>Good practice statement</p>

N.º	RECOMENDATION
7	<p>In adult patients with COVID-19 with acute respiratory distress syndrome (ARDS) and with respiratory failure, hypoxemia, or shock (who are not intubated or receiving mechanical ventilation), supplementary oxygen should be given immediately until SpO₂ is ≥94%.</p> <p>Strong recommendation. Certainty of the evidence: moderate</p>
8	<p>In adult patients with COVID-19 and acute hypoxemic respiratory failure who are receiving supplemental oxygen, SpO₂ should be maintained at no higher than 96%.</p> <p>Strong recommendation. Certainty of the evidence: moderate</p>
9	<p>In adult patients with COVID-19 and acute hypoxemic respiratory failure requiring supplemental oxygen, it is suggested to use noninvasive interphase ventilation or high-flow nasal oxygen, according to availability, in order to reduce mortality and likelihood of intubation.</p> <p>Conditional recommendation. Certainty of the evidence: very low</p>
✓	<p>In patients with respiratory distress who present with progressive acute hypoxemic respiratory failure and who do not respond to oxygen therapy via mask (flow rate 10–15 L/min: minimum flow to maintain the inflation pocket; FiO₂ 0.60–0.95), it is recommended to provide non-invasive mechanical ventilation or high-flow nasal cannula; otherwise, invasive mechanical ventilation.</p> <p>Good practice statement</p>
✓	<p>Oxygen therapy with high-flow nasal cannulae (HFNC) and non-invasive ventilation (NIMV) should be limited to units where patients with suspected or confirmed COVID-19 are hospitalized, and should be used only if the area is adequately ventilated or has a negative pressure system and if all staff in the area use correct airborne precautions. If this is not possible, it is preferable to use mechanical ventilation with orotracheal intubation.</p> <p>Good practice statement</p>
10	<p>In mechanically ventilated adult patients with COVID-19 and ARDS, it is recommended to use low tidal volume ventilation (4–8 mL/kg of predicted body weight) and to maintain plateau pressures of <30 cm H₂O. It is necessary to apply deep sedation to patients in order to achieve the proposed goals.</p> <p>Strong recommendation. Certainty of the evidence: moderate</p>
11	<p>For mechanically ventilated adult patients with COVID-19 and ARDS, a conservative strategy of positive end-expiratory pressure (PEEP) should be applied to prevent barotrauma.</p> <p><i>(If using a higher PEEP strategy, personnel should monitor patients who do not respond to higher PEEP levels for risk of barotrauma).</i></p> <p>Conditional recommendation. Certainty of the evidence: low</p>
12	<p>For mechanically ventilated adult patients with COVID-19 and ARDS, it is suggested to use a conservative fluid administration strategy rather than a liberal strategy.</p> <p>Strong recommendation. Certainty of the evidence: low</p>

N.º	RECOMENDATION
✓	<p>In patients with severe ARDS ($\text{PaO}_2/\text{FiO}_2 < 150$) and COVID-19, neuromuscular blockade by continuous infusion should not be used.</p> <p>Good practice statement</p>
13	<p>For mechanically ventilated adult patients with COVID-19 and moderate to severe ARDS, prone ventilation for 12 to 16 hours is suggested, as opposed to non-prone ventilation.</p> <p>Conditional recommendation. Certainty of the evidence: low</p>
✓	<p>The prone position should be considered in mechanically ventilated patients if PEEP is greater than 10 cm H₂O and the $\text{PaO}_2/\text{FiO}_2$ ratio is less than 150. The prone position requires sufficient human resources and expertise to carry out the procedure safely and in a standardized manner.</p> <p>Good practice statement</p>
✓	<p>The prone position is not recommended for patients with hemodynamic instability, unmonitored increase in intracranial pressure, or spinal instability.</p> <p>Good practice statement</p>
14	<p>For mechanically ventilated adult patients with COVID-19 and moderate to severe ARDS:</p> <ul style="list-style-type: none"> • Intermittent boluses of neuromuscular blocking agents (NMBA) are suggested, rather than continuous NMBA infusion, in order to facilitate protective lung ventilation. • In the event of persistent ventilator dyssynchrony, there may be a need for ongoing deep sedation, prone ventilation, or persistently high plateau pressures, using a continuous NMBA infusion for up to 48 hours. <p>Conditional recommendation. Certainty of the evidence: low</p>
15	<p>In mechanically ventilated adult patients with COVID-19 and ARDS, the use of inhaled nitric oxide is not recommended.</p> <p>Strong recommendation against. Certainty of the evidence: low</p>
16	<p>For mechanically ventilated adult patients with COVID-19 and refractory hypoxemia despite optimized ventilation, the use of recruitment maneuvers is recommended; incremental PEEP (gradual increases in PEEP) is not recommended.</p> <p>Strong recommendation. Certainty of the evidence: moderate</p>
17	<p>In adult patients with COVID-19 with or without ARDS or acute hypoxemic respiratory failure in need of supplemental oxygen, prone position is recommended for at least 3 hours. It should not be maintained if the patient reports discomfort or oxygenation does not improve. This is evaluated within the first 15 minutes of placing the patient in prone position.</p> <p>Conditional recommendation. Certainty of the evidence: very low</p>

N.º	RECOMENDATION
<p>18</p>	<p>In adult patients who produce or retain secretions and/or have a weak cough, it is suggested to use secretion removal techniques (e.g. postural drainage or respiratory flow acceleration maneuvers) to promote airway cleanliness and improve the safety of health professionals. Mechanical devices should not be used.</p> <p>Conditional recommendation. Certainty of the evidence: very low</p>
<p></p>	<p>It is recommended to avoid disconnecting the patient from the ventilator, given the loss of PEEP, risk of atelectasis, and increased risk of contagion of health professionals.</p> <p>Good practice statement</p>
<p>19</p>	<p>It is suggested to avoid delaying endotracheal intubation in patients with high-flow nasal oxygen (HFNO) or non-invasive ventilation (NIV) if their condition deteriorates or if they present PaO₂/FiO₂ ratios of 150 mmHg or lower in a short time period (1-2 hours).</p> <p>Conditional recommendation. Certainty of the evidence: very low</p>
<p></p>	<p>Extracorporeal membrane oxygenation (ECMO), if available, or referral of patients with refractory hypoxemia (e.g., ratio of partial pressure arterial oxygen [PaO₂] to the fraction of inspired oxygen [FiO₂] < 50mmHg for 3 hours, and PaO₂:FiO₂ < 80 mmHg for > 6 hours) should be considered, despite lung-protective ventilation.</p> <p>Good practice statement</p>

QUESTION 6.

HOW SAFE AND EFFECTIVE ARE INTERVENTIONS FOR HEMODYNAMIC SUPPORT OF CRITICALLY ILL PATIENTS WITH COVID-19?

*Updated question

N.º	RECOMENDATION
<p>20</p>	<p>For the acute resuscitation of adults with COVID-19 and shock, a conservative fluid administration strategy is suggested, rather than a liberal strategy.</p> <p>Conditional recommendation. Certainty of the evidence: very low</p>

N.º	RECOMENDATION
21	<p>In adults with COVID-19 and shock, various dynamic parameters should be used to assess fluid responsiveness. The following may be useful: stroke volume variation, pulse pressure variation, skin temperature, capillary refilling time, and/or serum lactate measurement.</p> <p>Conditional recommendation. Certainty of the evidence: low</p>
22	<p>For the acute resuscitation of adults with COVID-19 and shock, the administration of 250–500 mL of a crystalloid solution is recommended, rather than a colloid solution. Crystalloid solutions include normal saline solution and Ringer's lactate.</p> <p>Strong recommendation. Certainty of the evidence: low</p>
23	<p>For the acute resuscitation of adults with COVID-19 and shock, buffered/balanced crystalloids should be used, if available, rather than unbalanced crystalloids. Balanced crystalloid solutions include lactate, Ringer's, or other multi-electrolytic solutions.</p> <p>Conditional recommendation. Certainty of the evidence: low</p>
✓	<p>Fluid administration can lead to volume overload, including respiratory failure, particularly with ARDS. If there is no response to fluid loading or signs of overload appear (jugular venous distension, crackles on lung auscultation, pulmonary edema on imaging or hepatomegaly), reduce or discontinue fluid administration.</p> <p>Good practice statement</p>
24	<p>For the acute resuscitation of adults with COVID 19 and shock, we recommend against the use of hydroxyethyl starches, gelatins, or dextrans.</p> <p>Strong against recommendation. Certainty of the evidence: low</p>
25	<p>For the acute resuscitation of adults with COVID 19 and shock, we suggest against the routine use of albumin.</p> <p>Conditional recommendation. Certainty of the evidence: low</p>

QUESTION 7.

HOW SAFE AND EFFECTIVE ARE VASOPRESSORS AND CORTICOSTEROIDS FOR THE TREATMENT OF SEVERELY AND CRITICALLY ILL PATIENTS WITH COVID-19 IN SHOCK?



*Updated question

N.º	RECOMENDATION
26	<p>For adult patients with COVID19 and shock, norepinephrine should be used as the first-line vasoactive agent, rather than other agents.</p> <p>Conditional recommendation. Certainty of the evidence: low</p>
27	<p>For adult patients with COVID-19 and shock, if norepinephrine is not available, either vasopressin or epinephrine should be used as the first-line vasoactive agent, rather than other vasoactive agents.</p> <p>Conditional recommendation. Certainty of the evidence: low</p>
28	<p>For adults with COVID-19 and shock, the administration of dopamine is not recommended, given its low safety profile compared with the other vasopressors.</p> <p>Strong recommendation against. Certainty of the evidence: moderate</p>
29	<p>For adults with COVID 19 and shock, titrating vasoactive agents should be used to achieve a mean arterial pressure (MAP) of 60–65 mmHg, rather than higher MAP targets.</p> <p>Conditional recommendation. Certainty of the evidence: low</p>
30	<p>For adults with COVID 19 and shock, vasopressin should be added as a second-line agent if the target MAP cannot be achieved by norepinephrine alone.</p> <p>Conditional recommendation. Certainty of the evidence: moderate</p>
31	<p>For adults with COVID-19 and shock with signs of cardiac dysfunction and persistent hypoperfusion despite fluid resuscitation and norepinephrine, dobutamine should be added (with prior echocardiography), rather than increasing the norepinephrine dose.</p> <p>Conditional recommendation. Certainty of the evidence: very low</p>
32	<p>For adult patients with COVID-19 and shock who require the addition of a second vasopressor, low-dose corticosteroid therapy is suggested.</p> <p>Conditional recommendation. Certainty of the evidence: low</p>
✓	<p>Vasopressors should be administered to COVID-19 patients when shock persists during or after fluid resuscitation to achieve target MAP and improve perfusion markers. If central venous catheters (CVC) are not available, vasopressors can be administered through a peripheral intravenous catheter (for a short time, at low doses), using a large vein and closely monitoring for signs of extravasation and tissue necrosis, until a CVC can be placed. Whenever possible, a CVC should be inserted in the first 24–48 hours of vasopressor use.</p> <p>Good practice statement</p>

QUESTION 8.

HOW USEFUL IS DIAGNOSTIC IMAGING IN GUIDING TREATMENT OF CRITICALLY ILL PATIENTS WITH COVID-19?



*Updated question

N.º	RECOMENDATION
	<p>For hospitalized patients with severe symptoms (high risk of disease progression, unresponsive to supplemental oxygen treatment, or clinical suspicion of pulmonary fibrosis, pulmonary thromboembolism, or coronary thrombosis), diagnostic imaging is suggested to guide treatment, in addition to clinical and laboratory evaluation.</p> <p>Conditional recommendation. Certainty of the evidence: low</p>
	<p>The type of diagnosis should be selected based on availability, location of the deterioration, type of patient (mechanical ventilation), and preferential diagnosis. Chest CT scans or x-rays, and lung ultrasounds are preferred.</p> <p>Good practice statement</p>

QUESTION 9.

HOW SAFE AND EFFECTIVE ARE PHARMACOLOGICAL INTERVENTIONS FOR THE TREATMENT OF SEVERELY AND CRITICALLY ILL PATIENTS WITH COVID-19 IN INTENSIVE CARE UNITS?

*Updated question

N.º	RECOMENDATION
	<p>It is recommended not to use remdesivir, lopinavir/ritonavir, ivermectin, chloroquine, or hydroxychloroquine--with or without azithromycin, colchicine, and convalescent plasma--for the management of COVID-19 patients or in clinical trials.</p> <p>Strong recommendation against. Certainty of the evidence: moderate and low</p>
	<p>Use of tocilizumab is suggested in severely and critically ill patients admitted to intensive care units, due to rapid respiratory decompensation.</p> <p>Conditional recommendation. Certainty of the evidence: low</p>



N.º	RECOMENDATION
36	<p>Administration of antiparasitics, antivirals, n-acetylcysteine, and immunomodulators (except tocilizumab) is not suggested outside of clinical trials.</p> <p>Conditional recommendation against. Certainty of the evidence: very low</p>
37	<p>Use of baricitinib is suggested in severely and critically ill patients admitted to intensive care units, due to rapid respiratory decompensation.</p> <p>Conditional recommendation. Certainty of the evidence: low</p>
38	<p>Administering corticosteroids at low doses to severely and critically ill patients who are on supplementary oxygen or on a ventilator is recommended to reduce mortality and progression to invasive mechanical ventilation.</p> <p>Strong recommendation for. Certainty of the evidence: moderate</p>
39	<p>It is recommended not to use sotrovimab and casirivimab or imdevimab in severely or critically ill patients with COVID-19.</p> <p>Strong recommendation against. Certainty of the evidence: moderate and low</p>
40	<p>In mechanically ventilated adult patients with COVID-19, it is suggested to use empiric antimicrobials/antibacterial agents for 5 to 7 days, following institutional protocols and considering the clinical diagnosis (e.g., community-acquired pneumonia, sepsis, or suspected associated bacterial infection) and local data on bacterial resistance.</p> <p>Conditional recommendation. Certainty of the evidence: low</p>
✓	<p>Administration of antibiotics should be initiated within an hour of assessing the patient. Antibiotic therapy should be deescalated on the basis of microbiological results and clinical judgment.</p> <p>Good practice statement</p>
✓	<p>A long-term rehabilitation program should be established at the time of discharge from the ICU; with referral to specialized rehabilitation services or centers that care for COVID-19 patients who remain infectious. Consideration should be given to carrying out the program activities virtually.</p> <p>Good practice point</p>
41	<p>In adult patients with COVID-19 who develop fever, drugs should be used for temperature control. The choice of drug will depend on each patient's comorbidities.</p> <p>Conditional recommendation. Certainty of the evidence: low</p>
42	<p>It is suggested not to administer NSAIDs to severely or critically ill patients with COVID-19, in order to reduce pleuropulmonary complications.</p> <p>Conditional recommendation against. Certainty of the evidence: very low</p>

QUESTION 10.

WHAT ARE THE GUIDELINES FOR PREVENTION OF COMPLICATIONS ASSOCIATED WITH THE TREATMENT OF CRITICALLY ILL PATIENTS WITH COVID-19?

*Updated question

N.º	RECOMENDATION
<p>43</p>	<p>In critically ill patients without contraindication to anticoagulants, pharmacological prophylaxis, such as low molecular weight heparin (LMWH), is recommended, in accordance with local and international standards, to prevent venous thromboembolism. For patients with contraindications, it is suggested the use of mechanical prophylaxis (intermittent pneumatic compression devices).</p> <p>Strong recommendation. Certainty of the evidence: very low</p>
<p>✓</p>	<p>Patients at high risk of thromboembolism should be identified according to the following markers: high levels of C-reactive protein, fibrinogen, and D-dimer. Critically ill patients with COVID-19 and high risk of thromboembolism, without kidney complications and at low risk of bleeding, should receive 1 mg/kg of enoxaparin per day for at least 7 days. Side effects and markers should be tracked if decreasing enoxaparin to 40 mg.</p> <p>Good practice statement</p>
<p>✓</p>	<p>Prophylactic therapy should be initiated within the first 14 hours of admission and continued for 7 days or for the duration of the hospital stay. If patients are receiving anticoagulation therapy at the time of admission to ICU, the established therapeutic regimen should be continued.</p> <p>Good practice statement</p>
<p>44</p>	<p>The use of proton pump inhibitors is suggested in selected patients with continued vasopressor use, at prophylactic doses for short periods of time, to prevent bleeding from stress ulcers. Patients should be monitored for risk of healthcare-associated infections (HAIs).</p> <p>Conditional recommendation. Certainty of the evidence: very low</p>
<p>✓</p>	<p>Drug interactions and side effects of administered medications that may affect COVID-19 symptoms (including effects on respiratory, cardiac, neurological, mental, and immune functions) should be carefully considered.</p> <p>Good practice statement</p>

N.º	RECOMENDATION
	<p>The following interventions are recommended to prevent complications associated with the management of critically ill patients with COVID-19:</p> <p>Reduce the incidence of ventilator-associated pneumonia</p> <ul style="list-style-type: none"> • Use an institutional protocol for ventilator weaning that includes daily assessment. • Select oral intubation over nasal intubation in adolescents and adults. • Keep the patient in a semi-recumbent position (head elevation of 30°–45°). • Use a closed suctioning system; periodically drain and discard condensate in tubing. • Use a new ventilator circuit for each patient; once the patient is ventilated, change the circuit if soiled or damaged, but not routinely. • Change the heat moisture exchanger when it malfunctions, when soiled, or every 5–7 days. <p>Reduce the incidence of blood infections associated with intravenous devices</p> <ul style="list-style-type: none"> • Use a checklist as a reminder of each step needed for sterile insertion and as a daily reminder to remove the intravenous device if no longer needed. <p>Reduce the incidence of pressure ulcers</p> <ul style="list-style-type: none"> • Turn the patient on his/her side every two hours. • Actively mobilize the ill patient when safe to do so. <p>Reduce the incidence of stress ulcers and gastrointestinal bleeding</p> <ul style="list-style-type: none"> • Give early enteral nutrition (within 24-48 hours of admission). <p>Good practice statement</p>
	<p>Identifying and managing possible underlying causes of delirium (often multicausal) is key; as well as periodic assessments of risk factors, prompt mobilization and reorientation of the patient, and standardization of the sleep-wake cycle. Ensure effective communication with patients, calm them, and involve family members and caregivers virtually.</p> <p>Good practice statement</p>
45	<p>Administration of a low initial dose of haloperidol (0.5 mg up to a maximum of 10 mg/day) is suggested for ICU patients with delirium who are unresponsive to nonpharmacological interventions to manage delirium (reorientation, schedules, clocks, natural lighting, reduce ambient noise, facilitate sleep, avoid drugs with deliriogenic potential, etc.).</p> <p>Conditional recommendation. Certainty of the evidence: very low</p>

N.º	RECOMENDATION
46	<p>Monitoring and management of the following neurological and cardiac manifestations is suggested for critical patients: headaches, confusion, altered level of consciousness, peripheral nervous system symptoms, cerebrovascular events, and epilepsy.</p> <p>Conditional recommendation. Certainty of the evidence: very low</p>

QUESTION 11.**WHAT IS THE EFFICACY AND SAFETY OF EARLY REHABILITATION FOR PATIENTS WITH COVID-19 IN INTENSIVE CARE UNITS?**





*Updated question

N.º	RECOMENDATION
47	<p>For patients hospitalized in the ICU with COVID-19, early rehabilitation is suggested to reduce weakness acquired while in ICU.</p> <p>Conditional recommendation. Certainty of the evidence: very low</p>
✓	<p>The type of early rehabilitation depends on the patient, type of ventilation, whether the patient is sedated, and the resources available in the facility.</p> <p>Good practice statement</p>

QUESTION 12.**WHAT ARE THE REQUIREMENTS FOR DISCHARGE OF COVID-19 PATIENTS FROM THE INTENSIVE CARE UNIT?**

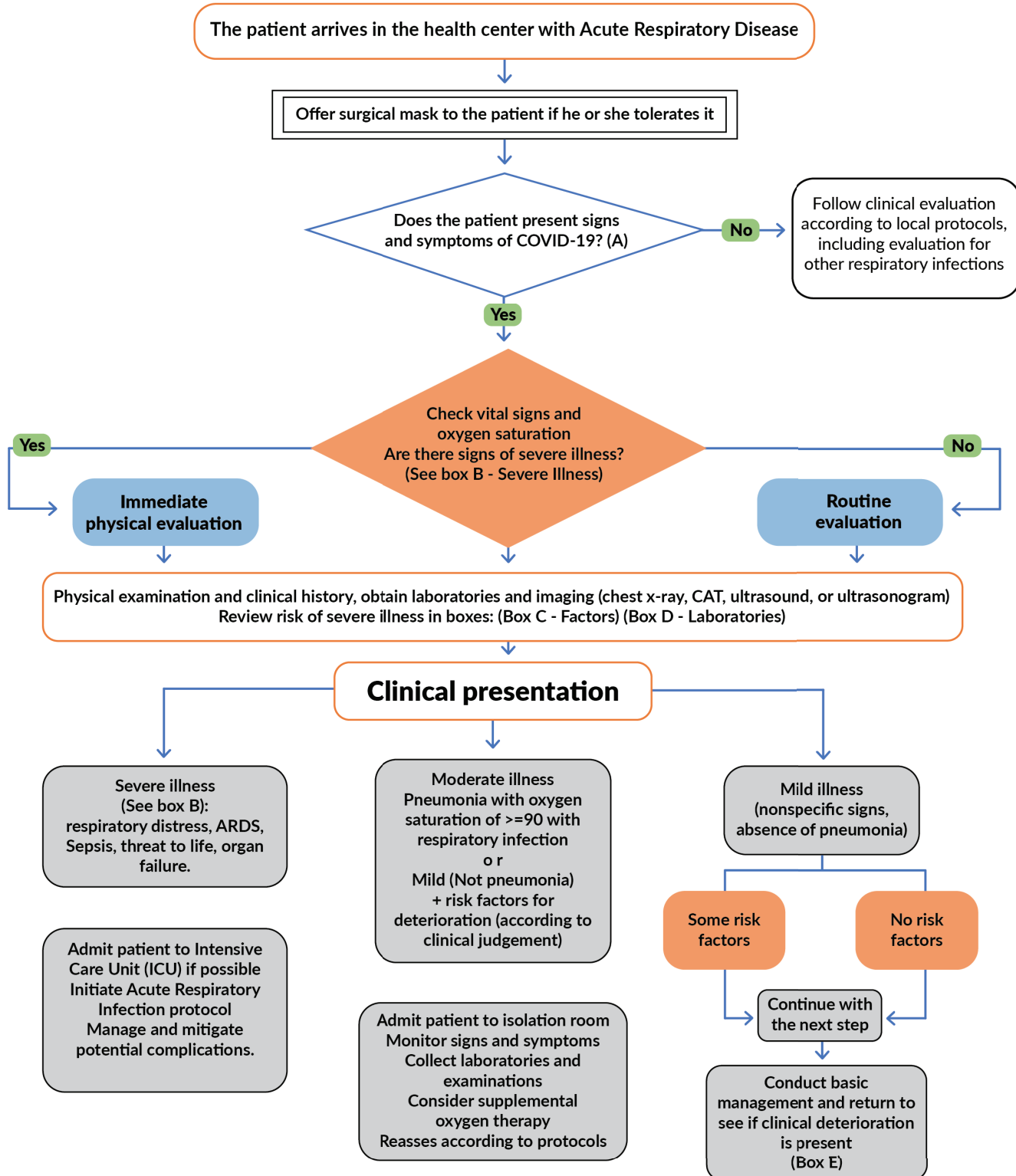
*Updated question

N.º	RECOMENDATION
48	<p>For patients hospitalized in the ICU with COVID-19 whose symptoms have improved, a clinical, laboratory evaluation, it is suggested to be performed to verify that no respiratory, renal, or hemodynamic support is required, before making the decision to discharge patients from the unit.</p> <p>Strong recommendation. Certainty of the evidence: very low</p>
49	<p>For patients receiving oral anticoagulants prior to ICU admission, it is recommended to make a risk stratification of developing venous thromboembolism after discharge and to consider extending prophylaxis using standard doses.</p> <p>Strong recommendation. Certainty of the evidence: very low</p>

N.º	RECOMENDATION
	<p>For patients who have been discharged from the intensive care unit, it is recommended to evaluate swallowing, mobility, delirium, cognitive decline, and mental health. Based on the evaluation, rehabilitation and follow-up requirements are determined.</p> <p>Good practice statement</p>
	<p>Patients who meet the ICU's discharge requirements, it is suggested to leave with an exit plan that includes a summary of the diagnosis upon discharge, medications, and a care plan. The patient and their family should also receive information about their care.</p> <p>Conditional recommendation. Certainty of the evidence: very low</p>
	<p>A rehabilitation program (from discharge to long term) should be developed after discharge from the intensive care unit; with referral to specialized rehabilitation services or centers designed to care for patients with COVID-19 who remain infectious. Consider performing scheduled activities virtually.</p> <p>Good practice statement</p>
	<p>Rehabilitation programs should be implemented by multidisciplinary teams and should be geared around patient needs and goals, including physical therapy; education and advice on self-care strategies; breathing techniques; support for caregivers; support groups, stress management, and home modifications.</p> <p>Good practice statement</p>

ALGORITHMS

FLOWCHART FOR CLINICAL MANAGEMENT OF COVID-19



*See boxes on the next page

FLOW CHART FOR CLINICAL MANAGEMENT COVID-19 BOXES

BOX A:

Common COVID-19 symptoms

- Fever
- Cough + Sputum
- Breathlessness
- Muscle pain (Myalgia)
- Fatigue
- Nausea/Vomiting
- Cold
- Diarrhea
- Headache
- Sore throat
- Vasculitic rash

BOX B:

Signs of severe illness

- Respiratory rate > 30
- Pulse > 100
- Hypotension
- Arrhythmia
- Evidence of dyspnea (muscular, cervical, or intercostal retraction, nostril flaring, cyanosis, oxygen saturation < 94% or based on clinical.)

BOX C:

Factors

- Atherosclerosis
- Cancer
- Diabetes
- Males
- Cardiovascular disease
- Liver disease
- Neurological disease
- Pulmonary disease
- Kidney disease
- Hypertension
- Immunodeficiency for any reason
- Obesity
- People over 60 years of age

BOX D:

Routine laboratory tests according to availability

- Respiratory specimens for viral assessment of COVID-19
- Liver function
- Blood count
- Other laboratory tests based on local epidemiology (influenza, other respiratory infections, dengue, malaria)
- Urine analysis

Additional laboratory tests according to availability

- Procalcitonin
- CPK
- D-dimer and fibrinogen
- C-reactive protein

Diagnostic imaging according to availability

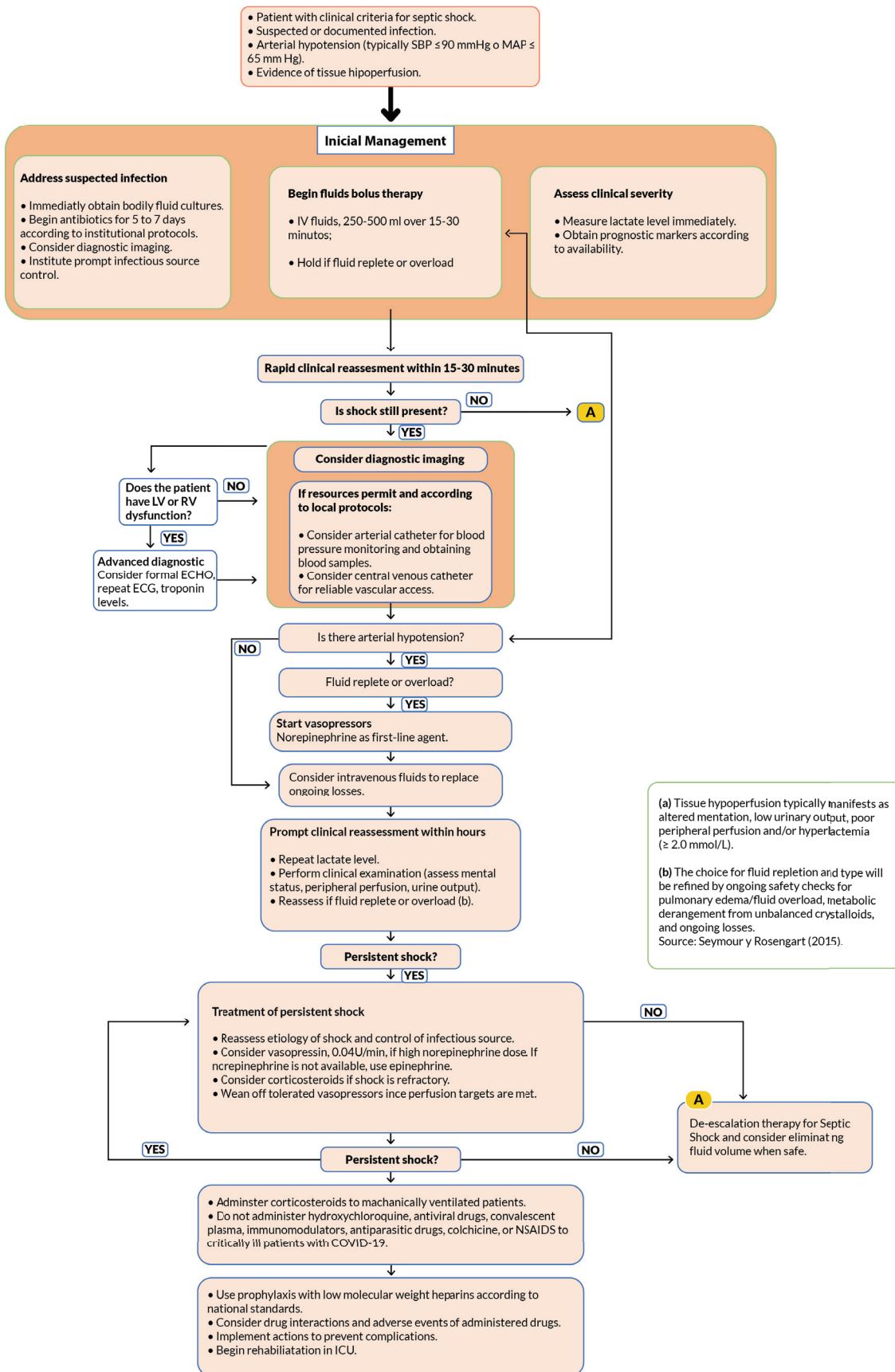
- Chest x-ray
- Chest CT scan

BOX E:

Signs of deterioration

- Increase in difficulty breathing
- Drop in blood pressure
- Blue coloration in lips and face
- Confusion or lack of ability to rise
- Increase weakness
- Reduction of oxygen saturation to less than 90%
- Persistent chest pain
- Reddening or inflammation of the limbs
- Dizziness
- Loss of consciousness
- Respiratory rate higher than 20

PROPOSED ALGORITHM FOR TREATMENT OF CRITICALLY ILL PATIENTS WITH SEPTIC SHOCK



WHO AND PAHO GUIDELINES TO SUPPORT THIS DOCUMENT

- Requirements and technical specifications of personal protective equipment (PPE) for the novel coronavirus (2019-nCoV) in healthcare settings

<https://iris.paho.org/bitstream/handle/10665.2/51905/requirements-%20PPE-coronavirus-spa.pdf?sequence=1&isAllowed=y>

- Technical specifications of medical devices for the case management of COVID-19 in healthcare settings

<https://www.paho.org/es/documentos/especificaciones-tecnicas-dispositivos-medicos-para-gestion-casos-covid-19-servicios>

- Presentation: Infection Prevention and Control and novel coronavirus (COVID-19): standard precautions and use of personal protective equipment

<https://www.paho.org/en/documents/presentation-infection-prevention-and-control-and-novel-coronavirus-covid-19-standard>

- Interim laboratory biosafety guidelines for the handling and transport of samples associated with the novel coronavirus 2019 (2019-nCoV)

<https://www.paho.org/en/documents/interim-laboratory-biosafety-guidelines-handling-and-transport-samples-associated-novel>

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

[https://www.who.int/publications-detail/infection-prevention-and-control-during-health-care-when-novel-coronavirus-\(ncov\)-infection-is-suspected-20200125](https://www.who.int/publications-detail/infection-prevention-and-control-during-health-care-when-novel-coronavirus-(ncov)-infection-is-suspected-20200125)

Natural ventilation for infection control in healthcare settings

https://www.paho.org/hq/dmdocuments/2011/ventilacion_natural_spa_25mar11.pdf

DIAGNOSIS OF COVID-19

- Coronavirus disease (COVID-19) technical guidance: Laboratory testing for 2019-nCoV in humans

<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/laboratory-guidance>

- Laboratory testing for 2019 novel coronavirus (2019-nCoV) in suspected human cases

<https://www.who.int/publications-detail/laboratory-testing-for-2019-novel-coronavirus-in-suspected-human-cases-20200117>

- Guidance for laboratories shipping specimens to WHO reference laboratories that provide confirmatory testing for COVID-19 virus

https://apps.who.int/iris/bitstream/handle/10665/331639/WHO-2019-nCoV-laboratory_shipment-2020.3-eng.pdf

TREATMENT

- COVID-19 Clinical management: living guidance

<https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2021-1>

- Home care for patients with suspected novel coronavirus (2019-nCoV) infection presenting with mild symptoms and management of contacts

[https://www.who.int/publications-detail/home-care-for-patients-with-suspected-novel-coronavirus-\(ncov\)-infection-presenting-with-mild-symptoms-and-management-of-contacts](https://www.who.int/publications-detail/home-care-for-patients-with-suspected-novel-coronavirus-(ncov)-infection-presenting-with-mild-symptoms-and-management-of-contacts)

- COVID-19: Chloroquine and hydroxychloroquine research

<https://iris.paho.org/handle/10665.2/52105>

- Essential medicines list for the management of patients admitted to intensive care units with suspected or confirmed COVID-19 diagnosis.

<https://iris.paho.org/handle/10665.2/52640>

- List of Priority Medical Devices in the Context of COVID-19

<https://iris.paho.org/handle/10665.2/52580>

GLOBAL MONITORING OF COVID-19

- Global Surveillance for human infection with coronavirus disease (COVID-19)

[https://www.who.int/publications-detail/global-surveillance-for-human-infection-with-novel-coronavirus-\(2019-ncov\)](https://www.who.int/publications-detail/global-surveillance-for-human-infection-with-novel-coronavirus-(2019-ncov))

- Revised case report form for Confirmed Novel Coronavirus COVID-19 (report to WHO within 48 hours of case identification)

<https://apps.who.int/iris/bitstream/handle/10665/331234/WHO-2019-nCoV-SurveillanceCRF-2020.2-eng.pdf>

DISCHARGE OF RECOVERED PATIENTS

- Clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) infection is suspected

[https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-\(ncov\)-infection-is-suspected](https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected)

- Novel coronavirus (SARS-CoV-2) Discharge criteria for confirmed COVID-19 cases – When is it safe to discharge COVID-19 cases from the hospital or end home isolation?

<https://www.ecdc.europa.eu/sites/default/files/documents/COVID-19-Discharge-criteria.pdf>

CONSIDERATIONS FOR INVESTIGATION AND HEALTH SERVICES

- Considerations for Strengthening the First Level of Care in the Management of the COVID-19 Pandemic

<https://iris.paho.org/handle/10665.2/53190>

- Considerations in the investigation of cases and clusters of COVID-19

<https://www.who.int/publications-detail/considerations-in-the-investigation-of-cases-and-clusters-of-covid-19>

- Operational considerations for case management of COVID-19 in health facility and community

https://apps.who.int/iris/bitstream/handle/10665/331492/WHO-2019-nCoV-HCF_operations-2020.1-eng.pdf

- Reorganization and Progressive Expansion of Health Services for the Response to the COVID-19 Pandemic

<https://www.paho.org/en/documents/reorganization-and-progressive-expansion-health-services-response->

[covid-19-pandemic](#)

• **Severe Acute Respiratory Infections Treatment Centre**

<https://www.who.int/publications-detail/severe-acute-respiratory-infections-treatment-centre>

• **COVID-19 v4. Operational Support & Logistics. Disease Commodity Packages.**

https://www.who.int/docs/default-source/coronaviruse/dcp-ncov-v4.pdf?sfvrsn=f5fe6234_7

• **Recommendations for Implementing the CICOM Methodology during the COVID-19 Response.**

<https://iris.paho.org/handle/10665.2/52376>

DEAD BODY MANAGEMENT

Dead body management in the context of the novel coronavirus (COVID-19)

<https://www.paho.org/es/documentos/manejo-cadaveres-contexto-nuevo-coronavirus-covid-19>

DEVELOPMENT GROUP

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