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# COVID-19 PREPAREDNESS AND RESPONSE PLAN FOR OUTBREAK CONTROL

## CLINICAL MANAGEMENT OF SEVERE ACUTE RESPIRATORY INFECTION WHEN NOVEL CORONAVIRUS COVID-19 INFECTION IS SUSPECTED

***March 2020 –Version 2***

## BACKGROUND

This clinical guidance for novel coronavirus, is an adaptation of World Health Organisation Clinical Management of Severe Acute Respiratory Infection when MERS-CoV infection is suspected (2019). This document is intended for clinicians taking care of hospitalised adult and paediatric patients with severe acute respiratory infection (SARI) when a COVID-19 infection is suspected. It is not meant to replace clinical judgment or specialist consultation but rather to strengthen clinical management of these patients and provide an up-to-date guidance. Best practices for SARI including Infection Prevention and Control (IPC) and optimized supportive care for severely ill patients are essential.

**These guidelines serve as interim guidelines and will be amended as the global and local situation evolves**.

This document is organized into the following sections:

1. Triage: recognize and sort patients with SARI
2. Immediate implementation of appropriate infection prevention and control (IPC) measures
3. Early supportive therapy and monitoring

4. Collection of specimens for laboratory diagnosis
5. Management of hypoxemic respiratory failure and acute respiratory distress syndrome (ARDS)
6. Management of septic shock
7. Prevention of complications
8. Specific anti-COVID-19 treatments
9. Special considerations for pregnant patients

These symbols are used to flag interventions:

- ✓ **Do:** the intervention is beneficial (strong recommendation) OR the intervention is a best practice statement
- ❖ **Don't:** the intervention is known to be harmful.
- **Consider:** the intervention may be beneficial in selected patients (conditional recommendation) OR be careful when considering this intervention.

This document aims to provide clinicians with updated interim guidance on timely, effective, and safe supportive management of patients with SARI associated with, particularly those with critical illness.

The recommendations in this document are derived from WHO publications.[1-4]

## 1. Triage: early recognition of patients with SARI associated with COVID-19 infection

- **Triage:** **Approach all patients with standard infection prevention and control (IPC) practices. Consider COVID-19 as a possible aetiology of SARI under certain conditions (see Table 1). Triage patients, isolate and start emergency treatment based on the disease severity.**

*Remarks:* COVID-19 may present with mild, moderate, or severe illness; the latter includes severe pneumonia, ARDS, sepsis and septic shock. Therefore, early recognition of suspected patients allows for timely initiation of contact and droplet precautions. Early identification of those with severe manifestations (see Table 2) allows for immediate optimized supportive care treatments and safe, rapid admission (or referral) to intensive care unit according to institutional or national protocols.

**In the event that an outbreak is declared: for those with mild illness, hospitalization may not be required unless there is concern for rapid deterioration.** All patients discharged home should be instructed to return to hospital if they develop any worsening of illness.

**Table 1. Definitions of patients with SARI, suspected of COVID-19***

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| **SARI** | Any case which presents with history of fever or measured temperature ≥38 °C and cough; onset within the last ~10 days; and requiring hospitalization.[5] |
| **Surveillance case definitions for COVID-19** | **Suspect case**<br>**A**<br>A person with acute respiratory illness (fever and at least ONE (1) sign or symptom of respiratory disease (e.g., Cough, Shortness of Breath)) AND with no other aetiology that fully explains the clinical presentation AND a history of travel to or residence in a country/area/territory reporting local transmission (see current WHO COVID-19 Situation Report) of COVID-19 disease in the 14 days prior to symptom onset.<br>**B**<br>A person with any acute respiratory illness AND having been in contact with a confirmed or probable case of COVID-19 case, in the 14 days prior to the onset of illness.<br>**C**<br>A person with severe acute respiratory infection (fever and at least ONE (1) sign or symptom of respiratory disease (e.g., Cough, Shortness of Breath)) AND requiring hospitalization AND with no other aetiology that fully explains the clinical presentation.<br><br>**Probable case**<br>A suspect case for whom testing for COVID-19 is inconclusive[1] or is tested positive using a pancoronavirus assay and without laboratory evidence of other respiratory pathogens.<br><br>**Confirmed case**<br>A person with laboratory confirmation of COVIV-19 infection, irrespective of clinical signs and symptoms |

**Table 2. Clinical syndromes associated with COVID-19 infection**

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| Uncomplicated illness | Patients with uncomplicated upper respiratory tract viral infection, may have non-specific symptoms such as fever, cough, sore throat, nasal congestion, malaise, headache, muscle pain. The elderly and immunocompromised may present with atypical symptoms. These patients do not have any signs of dehydration, sepsis or shortness of breath. |
| Mild pneumonia | Patient with pneumonia and no signs of severe pneumonia.<br>Child with non-severe pneumonia has cough or: fast breathing (in breaths/min): <2 months, ≥60; 2–11 months, ≥50; 1–5 years, ≥40 and no signs of severe pneumonia. |
| Severe pneumonia | Adolescent or adult: fever or suspected respiratory infection, plus one of respiratory rate >30 breaths/min, severe respiratory distress, or SpO2 <90% on room air (adapted from [1]).<br>Child with cough or difficulty in breathing, plus at least one of the following: central cyanosis or $SpO_2$ <90%; severe respiratory distress (e.g. grunting, very severe chest indrawing); signs of pneumonia with any of the following: general danger sign:<br>• inability to breastfeed or drink,<br>• lethargy or unconsciousness, or<br>• convulsions.<br>• Other signs of pneumonia may be present:<br>• chest indrawing,<br>• fast breathing (in breaths/min): <2 months, ≥60; 2–11 months, ≥50; 1–5 years, ≥40.[2] The diagnosis is clinical; chest imaging can exclude complications. |
| Acute Respiratory Distress Syndrome [7-9] | **Onset:** new or worsening respiratory symptoms within one week of known clinical insult. **Chest imaging (radiograph, CT scan, or lung ultrasound):** bilateral opacities, not fully explained by effusions, lobar or lung collapse, or nodules. |

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| | **Origin of oedema**: respiratory failure not fully explained by cardiac failure or fluid overload. Need objective assessment (e.g. echocardiography) to exclude hydrostatic cause of oedema if no risk factor present.<br><br>**Oxygenation (adults)**:<br>• Mild ARDS: 200 mmHg < $PaO_2/FiO_2$ ≤ 300 mmHg (with PEEP or CPAP ≥5 $cmH_2O$, or non-ventilated[8])<br>• Moderate ARDS: 100 mmHg < $PaO_2/FiO_2$ ≤200 mmHg with PEEP ≥5 $cmH_2O$, or non-ventilated[8])<br>• Severe ARDS: $PaO_2/FiO_2$ ≤ 100 mmHg with PEEP ≥5 $cmH_2O$, or non-ventilated[8])<br>• When $PaO_2$ is not available, $SpO_2/FiO_2$ ≤315 suggests ARDS (including in non-ventilated patients)<br>**Oxygenation (children; note OI = Oxygenation Index and OSI = Oxygenation Index using $SpO_2$):**<br>• Bilevel NIV or CPAP ≥5 $cmH_2O$ via full face mask: $PaO_2/FiO_2$ ≤ 300 mmHg or $SpO_2/FiO_2$ ≤264<br>• Mild ARDS (invasively ventilated): 4 ≤ OI < 8 or 5 ≤ OSI < 7.5<br>• Moderate ARDS (invasively ventilated): 8 ≤ OI < 16 or 7.5 ≤ OSI < 12.3<br>• Severe ARDS (invasively ventilated): OI ≥ 16 or OSI ≥ 12.3 |
| Sepsis [10,11] | **Adults:** life-threatening organ dysfunction caused by a dysregulated host response to suspected or proven infection, with organ dysfunction*. Signs of organ dysfunction include: altered mental status, difficult or fast breathing, low oxygen saturation, reduced urine output, fast heart rate, weak pulse, cold extremities or low blood pressure, skin mottling, or laboratory evidence of coagulopathy, thrombocytopenia, acidosis, high lactate or hyperbilirubinemia. |

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| | **Children:** suspected or proven infection and ≥2 SIRS criteria, of which one must be abnormal temperature or white blood cell count. |
| Septic shock [10,12] | **Adults:** persisting hypotension despite volume resuscitation, requiring vasopressors to maintain MAP ≥65 mmHg and serum lactate level >2 mmol/L.<br>**Children** any hypotension (SBP 2 SD below normal for age) or 2-3 of the following: altered mental state; tachycardia or bradycardia (HR 160 bpm in infants and HR 150 bpm in children); prolonged capillary refill (>2 sec) or warm vasodilation with bounding pulses; tachypnea; mottled skin or petechial or purpuric rash; increased lactate; oliguria; hyperthermia or hypothermia.[12] |

*NB: Patient may not have fever*

## 2. Immediate implementation of appropriate IPC measures

IPC is a critical and integral part of clinical management of patients and should be initiated at the point of entry of the patient to health care facility, (typically the Emergency Department).
Standard precautions should always be routinely applied in all areas of health care facilities.

Standard precautions include:

- hand hygiene;
- use of appropriate PPE (surgical mask, gloves, gown, face-shield, eye protection) to avoid direct contact with patients' blood, body fluids, secretions (including respiratory secretions) and non-intact skin.
- prevention of needle-stick or sharps injury;
- safe waste management;
- cleaning and disinfection of equipment; and

- cleaning of the environment.

**Table 3. How to implement infection prevention and control measures for patients with suspected or confirmed COVID-19 infection [14,15]**

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| At triage | Give suspect patient a medical mask and direct patient to a separate area, an isolation room if available. Keep at least 1-meter distance between suspected patients and other patients. Instruct all patients to cover nose and mouth during coughing or sneezing with tissue or flexed elbow for others. Perform hand hygiene after contact with respiratory secretions. |
| Apply droplet precautions | Droplet precautions prevent large droplet transmission of respiratory viruses.<br>• Use a medical mask if working within 1-2 metres of the patient.<br>• Place patients in single rooms, or group together those with the same aetiological diagnosis. If an aetiological diagnosis is not possible, group patients with similar clinical diagnosis and based on epidemiological risk factors, with a spatial separation.<br>• When providing care in close contact with a patient with respiratory symptoms (e.g. coughing or sneezing), **use droplet precautions gowns, gloves, airway protection (surgical mask) and eye protection (face-shield)** because sprays of secretions may occur.<br>• Limit patient movement within the institution and ensure that patients wear surgical masks when outside their rooms. |

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| Apply contact precautions | Droplet and contact precautions prevent direct or indirect transmission from contact with contaminated surfaces or equipment (i.e. contact with contaminated oxygen tubing/interfaces).<br>• Use PPE (surgical mask, face shields, gloves and gown) when entering room and remove PPE when leaving.<br>• If possible, use either disposable or dedicated equipment (e.g. stethoscopes, blood pressure cuffs and thermometers).<br>• If equipment needs to be shared among patients, clean and disinfect between each patient use.<br>• Avoid contaminating environmental surfaces that are not directly related to patient care (e.g. door handles and light switches).<br>• Ensure adequate room ventilation.<br>• Avoid movement of patients.<br>• Train Health care workers to refrain from touching their eyes, nose, and mouth with potentially contaminated gloved or ungloved hands.<br>• Perform hand hygiene. |
| Apply airborne precautions when performing an aerosol generating procedure | • Healthcare workers performing aerosol-generating procedures (i.e. open suctioning of respiratory tract, intubation, extubation, bronchoscopy, cardiopulmonary resuscitation) use PPE -gloves, long-sleeved impervious gowns, face shields, and fit-tested particulate respirators (N95 or equivalent, or higher level of protection). (The scheduled fit test should not be confused with user seal check before each use.) |

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| | • Whenever possible, use Airborne Infection Isolation rooms AIIR single rooms when performing aerosol-generating procedures. If not available, then increase the level of PPE to full coverage suits.<br>• Avoid the presence of unnecessary individuals in the room.<br>• Care for the patient in the same type of room after mechanical ventilation commences. |

*Abbreviations: ARI, acute respiratory infection; PPE, personal protective equipment*

### 3. Early supportive therapy and monitoring

✓ **Give supplemental oxygen therapy immediately to patients with SARI and respiratory distress, hypoxaemia, or shock.**

*Remarks:* Initiate oxygen therapy at 5 L/min and titrate flow rates to reach target $SpO_2$ ≥90% in non-pregnant adults and $SpO_2$ ≥92-95% in pregnant patients.[1,2] Children with emergency signs (obstructed or absent breathing, severe respiratory distress, central cyanosis, shock, coma or convulsions) should receive oxygen therapy during resuscitation to target $SpO_2$ ≥94%; otherwise, the target $SpO_2$ is ≥90%.[4] All areas where patients with SARI are cared for should be equipped with pulse oximeters, functioning oxygen systems and disposable, single-use, oxygen-delivering interfaces (nasal cannula, simple face mask, and mask with reservoir bag). Use contact precautions when handling contaminated oxygen interfaces of these patients.

✓ **Use conservative fluid management in patients with SARI when there is no evidence of shock.**

*Remarks:* Patients with SARI should be treated cautiously with intravenous fluids, because aggressive fluid resuscitation may worsen oxygenation, especially in settings where there is limited availability of mechanical ventilation.[16]

- ✓ **Give antimicrobials within one hour of initial patient assessment for patients with sepsis**. Give empiric antimicrobials to treat all likely pathogens causing SARI. (Azithromycin+ Amoxil-Clavuliinic Acid or Azithromycin+ Rocephin is a reasonably safe suggestion).

  *Remarks:* Although the patient may be suspected to have COVID-19, administer appropriate empiric antimicrobials within ONE hour of identification of sepsis.[17] Empiric antibiotic treatment should be based on the clinical diagnosis (community-acquired pneumonia, health care-associated pneumonia, or sepsis), local epidemiology, susceptibility data, and treatment guidelines. Empiric antiviral therapy including a neuraminidase inhibitor, may be considered. Empiric therapy should be de-escalated on the basis of microbiology results and clinical judgment.

- ❖ **Do not routinely give systemic corticosteroids for treatment of viral pneumonia or ARDS outside of clinical trials unless they are indicated for another reason.**

  *Remarks:* A systematic review of observational studies of corticosteroids administered to patients with SARS reported no survival benefit and possible harms (avascular necrosis, psychosis, diabetes, and delayed viral clearance).[19] A systematic review of observational studies in influenza found a higher risk of mortality and secondary infections with corticosteroids; the evidence was judged as very low to low quality due to confounding by indication.[20] A subsequent study that addressed this limitation by adjusting for time-varying confounders found no effect on mortality.[21] Finally, a recent study of patients receiving corticosteroids for MERS used a similar statistical approach and found no effect of corticosteroids on mortality but delayed lower respiratory tract (LRT) clearance of MERS-CoV. Given lack of effectiveness and possible harm, routine corticosteroids should be avoided unless they are indicated for another reason.

- ✓ **Closely monitor patients with SARI for signs of clinical deterioration, such as rapidly progressive respiratory failure and sepsis, and apply supportive care interventions immediately**.

*Remarks:* Application of timely, effective, and safe supportive therapies is the cornerstone of therapy for patients that develop severe manifestations of COVID-19.

- ✓ **Understand the patient's co-morbid condition(s) to tailor the management of critical illness and appreciate the prognosis. Communicate early with patient and family.**

  *Remarks:* During intensive care management of SARI, determine which chronic therapies should be continued and which therapies should be stopped temporarily. Communicate proactively with patients and families and provide support and prognostic information. Understand the patient's values and preferences regarding life-sustaining interventions.

## 4. Collection of specimens for laboratory diagnosis

WHO guidance on specimen, processing, and laboratory testing, including related biosafety procedures, is available.[23]

- ✓ **Collect blood cultures for bacteria that cause pneumonia and sepsis, ideally before antimicrobial therapy. DO NOT delay antimicrobial therapy to collect blood cultures.**

- ✓ **Collect specimens from BOTH the upper respiratory tract (URT; nasopharyngeal and oropharyngeal) AND lower respiratory tract (LRT; expectorated sputum, endotracheal aspirate, or bronchoalveolar lavage) for SARS CoV-2 testing by RT-PCR. Clinicians may elect to collect only LRT samples when these are readily available (for example, in mechanically ventilated patients).**

- ✓ **Serology for diagnostic purposes is recommended only when RT-PCR is not available.**[23]

  *Remarks:* Use appropriate PPE for specimen collection (droplet and contact precautions for URT specimens; airborne precautions for LRT specimens). When collecting URT samples, use viral swabs (sterile Dacron or rayon, not

cotton) and viral transport media. Do not sample the nostrils or tonsils. In a patient with suspected COVID-19 infection, especially with pneumonia or severe illness, a single URT sample does not exclude the diagnosis, and additional URT and LRT samples are recommended.[23] LRT (vs. URT) samples are more likely to be positive and for a longer period.[23] Clinicians may elect to collect only LRT samples when these are readily available (for example, in mechanically ventilated patients). Sputum induction should be avoided due to the risk of increasing aerosol transmission.

*Remarks:* Dual infections with other respiratory viral infections have been found in SARS, MERS and in COVID-19 cases. At this stage we need detailed microbiologic studies in all suspected cases. Both URT and LRT specimens can be tested for other respiratory viruses, such as influenza A and B (including zoonotic influenza A), respiratory syncytial virus, parainfluenza viruses, rhinoviruses, adenoviruses, enteroviruses (e.g. EVD68), human metapneumovirus, and endemic human coronaviruses (i.e. HKU1, OC43, NL63, and 229E). LRT specimens can also be tested for bacterial pathogens, including Legionella pneumophila. In hospitalized patients with confirmed COVID-19 infection, repeat URT and LRT samples should be collected to demonstrate viral clearance. The frequency of specimen collection will depend on the directives provided through the Emergency Operating Centre. Present recommendation is for at least every 2 to 4 days until there are two consecutive negative results (both URT and LRT samples if both are collected) in a clinically recovered patient at least 24 hours apart. If local infection control practice requires two negative results before removal of droplet precautions, specimens may be collected as often as daily.

## 5. Management of hypoxemic respiratory failure and ARDS

✓ **Recognize severe hypoxemic respiratory failure when a patient with respiratory distress is failing standard oxygen therapy.**

*Remarks:* Patients may continue to have increased work of breathing or hypoxemia even when oxygen is delivered via a face mask with reservoir bag (flow rates of 10-15 L/min, Hypoxemic respiratory failure in ARDS commonly results from intrapulmonary ventilation-perfusion mismatch or shunt and usually requires mechanical ventilation.

- **High-flow nasal oxygen (HFNO) or non-invasive ventilation (NIV) is not recommended with hypoxemic respiratory failure secondary to COVID-19.**
- *Remark 1 It is not recommended due to the high risk of aerosilation of the virus by this technique.*

✓ **Endotracheal intubation should be performed by a trained and experienced provider using airborne precautions.**

*Remarks:* Patients with ARDS, especially young children or those who are obese or pregnant, may desaturate quickly during intubation. Pre-oxygenate with 100% $FiO_2$ for 5 minutes, via a face mask with reservoir bag, bag-valve mask fitted with HEPA filter (otherwise there is a high probability of aerosol generation) . Rapid sequence intubation is the recommended technique after an airway assessment that identifies no signs of difficult intubation[32].

*The following recommendations in this section pertain to mechanically ventilated patients with ARDS [17,33] These focus on adults; consensus-based recommendations for children are available*. [34]

✓ **Implement mechanical ventilation using lower tidal volumes (4–8 ml/kg predicted body weight, PBW) and lower inspiratory pressures (plateau pressure <30 cmH2O).**

*Remarks:* This is a strong recommendation from a clinical guideline for patients with ARDS[33], and is suggested for patients with sepsis-induced respiratory failure

who do not meet ARDS criteria.[17] The initial tidal volume is 6 ml/kg PBW; tidal volume up to 8 ml/kg PBW is allowed if undesirable side effects occur (e.g. pH <7.15). Hypercapnia is permitted if meeting the pH goal of 7.30-7.45. The use of deep sedation may be required to control respiratory drive and achieve tidal volume targets.

- ✓ **In patients with severe ARDS, prone ventilation for >12 hours per day is recommended. This not currently available, but beds with lateral tilt may improve oxygenation.**

  *Remarks:* Application of prone ventilation is strongly recommended for adult and paediatric patients with severe ARDS but requires sufficient human resources and expertise to be performed safely.[37,38]

- ✓ **Use a conservative fluid management strategy for ARDS patients without tissue hypoperfusion.**

  *Remarks:* This is a strong guideline recommendation;[17] the main effect is to shorten the duration of ventilation. See reference [[39]] for details of a sample protocol.

- ✓ **In patients with moderate or severe ARDS, higher PEEP instead of lower PEEP is suggested.**

  *Remarks:* PEEP titration requires consideration of benefits (reducing atelectrauma and improving alveolar recruitment) vs. risks (end-inspiratory overdistension leading to lung injury and higher pulmonary vascular resistance). Tables are available to guide PEEP titration based on the $FiO_2$ required to maintain $SpO_2$.[35] A related intervention of recruitment manoeuvres (RMs) is delivered. Higher PEEP and RMs were both conditionally recommended in a clinical practice guideline.[33,41] Monitoring of patients to identify those who respond to the initial application of higher PEEP or a different RM protocol, and stopping these interventions in non-responders, is suggested.[42]

- ✓ **In patients with moderate-severe ARDS ($PaO_2/FiO_2$ <150), neuromuscular blockade by continuous infusion should not be routinely used.**

*Remarks:* One trial found that this strategy improved survival in patients with severe ARDS (PaO2/FiO2 <150) without causing significant weakness,[43] but results of a recent larger trial found that use of neuromuscular blockage with high PEEP strategy was not associated with survival when compared to a light sedation strategy without neuromuscular blockade[44]. Continuous neuromuscular blockade may still be considered in patients with ARDS in certain situations: ventilator dyssynchony despite sedation, such that tidal volume limitation cannot be reliably achieved; or refractory hypoxemia or hypercapnia.

- ✓ **Avoid disconnecting the patient from the ventilator, which results in loss of PEEP and atelectasis. Use in-line catheters for airway suctioning if available and clamp endotracheal tube when disconnection is required (for example, transfer to a transport ventilator).**

## 6. Management of septic shock

- ✓ **Recognize septic shock in adults when:**
  - infection is suspected or confirmed AND
  - vasopressors are needed to maintain mean arterial pressure (MAP) ≥65 mmHg AND
  - lactate is ≥2 mmol/L, in absence of hypovolemia.

- ✓ **Recognize septic shock in children with any hypotension (systolic blood pressure [SBP] <5th centile or >2 SD below normal for age) or 2-3 of the following:**
  - altered mental state;
  - tachycardia or bradycardia (HR <90 bpm or >160 bpm in infants and HR <70 bpm or >150 bpm in children);
  - prolonged capillary refill (>2 sec) or
  - warm vasodilation with bounding pulses;
  - tachypnea;
  - mottled skin or petechial or purpuric rash;
  - increased lactate;
  - oliguria;

- hyperthermia or hypothermia.

*Remarks:* In the absence of a lactate measurement, use MAP and clinical signs of perfusion to define shock. Standard care includes early recognition and the following treatments within 1 hour of recognition: antimicrobial therapy and fluid loading and vasopressors for hypotension.[49] The use of central venous and arterial catheters should be based on resource availability and individual patient needs. Detailed guidelines are available for the management of septic shock in adults[17] and children.[2,3,12]

✓ **In resuscitation from septic shock in adults, give at least 30 ml/kg of isotonic crystalloid in adults in the first 3 hours. In resuscitation from septic shock in children, give 20 ml/kg as a rapid bolus and up to 40-60 ml/kg in the first 1 hr.**

❖ **Do not use hypotonic crystalloids or starches, for resuscitation.**

**Fluid resuscitation may lead to volume overload, including respiratory failure. If there is no response to fluid loading and signs of volume overload appear (for example, jugular venous distension, crackles on lung auscultation, pulmonary oedema on imaging, or hepatomegaly in children), then reduce or discontinue fluid administration. This step is particularly important where mechanical ventilation is not available. Alternate fluid regimens are suggested when caring for children in resource-limited settings.**[50]

*Remarks:* Crystalloids include normal saline and Ringer's lactate. Determine need for additional fluid boluses (250-1000 ml in adults or 10-20 ml/kg in children) based on clinical response and improvement of perfusion targets. Perfusion targets include MAP (>65 mmHg or age-appropriate targets in children), urine output (>0.5 ml/kg/hr in adults, 1 ml/kg/hr in children), and improvement of skin mottling, capillary refill, level of consciousness, and lactate levels. Consider dynamic indices of volume responsiveness to guide volume administration beyond initial resuscitation based on local resources and experience.[17] These indices include passive leg raises, fluid challenges with serial stroke volume measurements, or variations in systolic pressure, pulse pressure, inferior vena

cava size, or stroke volume in response to changes in intrathoracic pressure during mechanical ventilation.

Starches are associated with an increased risk of death and acute kidney injury vs. crystalloids. The effects of gelatins are less clear, but they are more expensive than crystalloids.[51,52] Hypotonic (vs. isotonic) solutions are less effective at increasing intravascular volume. Surviving sepsis also suggests albumin for resuscitation when patients require substantial amounts of crystalloids, but this conditional recommendation is based on low-quality evidence.[17]

✓ **Administer vasopressors when shock persists during or after fluid resuscitation. The initial blood pressure target is MAP ≥65 mmHg in adults and age-appropriate targets in children.**

- **If central venous catheters are not available, vasopressors can be given through a peripheral IV, but use a large vein and closely monitor for signs of extravasation and local tissue necrosis. If extravasation occurs, stop infusion. Vasopressors can also be administered through intraosseous needles.**

- **If signs of poor perfusion and cardiac dysfunction persist despite achieving MAP target with fluids and vasopressors, consider an inotrope such as dobutamine.**

  *Remarks:* Vasopressors which can be used are:- norepinephrine, epinephrine, vasopressin, and dopamine. . Monitor blood pressure frequently and titrate the vasopressor to the minimum dose necessary to maintain perfusion andprevent side effects. Norepinephrine is considered first-line in adult patients; epinephrine or vasopressin can be added to achieve the MAP target. Because of the risk of tachyarrhythmia, reserve dopamine for selected patients with low risk of tachyarrhythmia or those with bradycardia. In children with cold shock (more common), epinephrine is considered first-line, while norepinephrine is used in patients with warm shock (less common).

  No RCTs have compared dobutamine to placebo for clinical outcomes.[17]

## 7. Prevention of complications

Implement the following interventions (Table 4) to prevent complications associated with critical illness. These interventions are based on Surviving Sepsis[17] or other guidelines, [54-57] and are generally limited to feasible recommendations based on high quality evidence.

**Table 4. Prevention of complications**

| Anticipated Outcome | Interventions |
|---|---|
| Reduce days of invasive mechanical ventilation | • Use weaning protocols that include daily assessment for readiness to breathe spontaneously<br>• Minimize continuous or intermittent sedation, targeting specific titration endpoints (light sedation unless contraindicated) or with daily interruption of continuous sedative infusions |
| Reduce incidence of ventilator- associated pneumonia | • Oral intubation is preferable to nasal intubation in adolescents and adults<br>• Keep patient in semi-recumbent position (head of bed elevation 30-45º)<br>• Use a closed suctioning system; periodically drain and discard condensate in tubing<br>• Use a new ventilator circuit for each patient; once patient is ventilated, change circuit if it is soiled or damaged but not routinely<br>• Change heat moisture exchanger when it malfunctions, when soiled, or every 5–7 days |
| Reduce incidence of venous thromboembolism | • Use pharmacological prophylaxis (low molecular-weight heparin [preferred if available] or heparin 5000 units subcutaneously 2-3 times daily) in adolescents and adults without contraindications. Use mechanical prophylaxis (intermittent pneumatic compression devices) is also recommended. |
| Reduce incidence of catheter-related bloodstream infection | • Use a checklist with completion verified by a real-time observer as reminder of each step needed for sterile insertion and as a daily reminder to remove catheter if no longer needed |
| Reduce incidence of pressure ulcers | • Turn patient every two hours. Use air mattress |
| Reduce incidence of stress ulcers and gastrointestinal bleeding | • Give early enteral nutrition (within 24–48 hours of admission) |

| Anticipated Outcome | Interventions |
|---|---|
| | • Administer proton-pump inhibitors in patients with risk factors for GI bleeding. Risk factors for gastrointestinal bleeding include mechanical ventilation for ≥48 hours, coagulopathy, renal replacement therapy, liver disease, multiple comorbidities, and higher organ failure score |
| Reduce incidence of ICU-related weakness | • Actively mobilize the patient early in the course of illness when safe to do so |

## 8. Specific anti COVID-19 treatments and clinical research

- **There is no current evidence from RCTs to recommend any specific anti-COVID-19 treatment for patients with suspected or confirmed COVID-19 infection.**

✓ **Unlicensed treatments should be administered only in the context of ethically-approved clinical trials or the Monitored Emergency Use of Unregistered Interventions Framework (MEURI), with strict monitoring.** https://www.who.int/ethics/publications/infectious-disease-outbreaks/en/

✓ **Clinical characterization protocols are available, at the WHO COVID-19 website:**
https://www.who.int/emergencies/diseases/novel-coronavirus-2019.
WHO has established Global 2019-nCoV Clinical Data Platform, for member countries to contribute. Contact EDCARN@who.int for additional questions.

## 9. Special considerations for pregnant patients

- ✓ **Pregnant women with suspected or confirmed 2019-nCoV infection should be treated with supportive therapies as described above, taking into account the physiologic adaptations of pregnancy.**

- ✓ **The use of investigational therapeutic agents outside of a research study should be guided by individual risk-benefit analysis based on potential benefit for mother and safety to foetus, with consultation from an obstetric specialist and ethics committee.**

- ✓ **Emergency delivery and pregnancy termination decisions are challenging and based on many factors: gestational age, maternal condition, and fetal stability. Consultations with obstetric, neonatal, and intensive care specialists (depending on the condition of the mother) are essential.**

- ✓ **A period of separation to prevent transmission by contact. If breastfeeding a mask is required plus strict adherence to contact precautions.**

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