

**INTERIM CLINICAL GUIDANCE FOR CARE OF PATIENTS WITH
COVID-19 IN HEALTHCARE SETTINGS**

NEPAL MEDICAL COUNCIL

(APRIL 3, 2020)

PREPARED BY:

NEPAL MEDICAL COUNCIL COVID-19 TREATMENT GUIDANCE COMMITTEE

ENDORSED BY:

NEPAL MEDICAL ASSOCIATION
SOCIETY OF INTERNAL MEDICINE OF NEPAL
NEPALESE SOCIETY OF CRITICAL CARE MEDICINE
GENERAL PRACTITIONERS ASSOCIATION OF NEPAL
NEPAL DENTAL ASSOCIATION

PUBLISHED BY:

NEPAL MEDICAL COUNCIL

KATHMANDU, NEPAL

Table of contents

	SECTIONS	PAGE NO.
I.	PURPOSE OF THE GUIDELINES	4
II.	TARGET GROUPS	4
III.	TRIAGING AND TRANSPORTATION OF PATIENTS	4
IV.	DIAGNOSIS	7
V.	TREATMENT	9
VI.	INFECTION PREVENTION AND CONTROL	20
VII.	REFERENCES	21
VIII.	APPENDICES	22
IX.	AUTHORS AND CONTRIBUTORS LIST	30

INTERIM CLINICAL GUIDANCE FOR CARING OF PATIENTS WITH COVID-19 IN HEALTHCARE SETTINGS

I. PURPOSE OF THE GUIDELINES

The purpose of these clinical guidelines document is to help physicians, other healthcare workers, healthcare institutions & policy makers to properly manage persons with suspected or proven COVID-19. COVID-19 (Coronavirus Infectious Disease 2019) is a respiratory tract infection caused by the betacoronavirus SARS CoV-2 (SARS coronavirus type-2). These guidelines are based on current knowledge in the available literature, expert consultations, and recommendations from WHO, CDC and other authorities. These guidelines are not meant to replace clinical judgment based on individual patient needs and do not exclude expert consultation and are subject to change based on new knowledge.

II. TARGET GROUPS

The intended target audience are physicians, nurses, other healthcare personnel, healthcare administration and policy makers involved in management of COVID-19 infection.

III. TRIAGING AND TRANSPORTATION OF PATIENTS

III.A. Who should be screened?

All persons including children and adults presenting to the outpatient clinics (OPD) and Emergency Room (ER) should be screened at the entrance of the hospital in a triage area.

III.B. How will the patients presenting to outpatient clinics (OPD) and Emergency Room (ER) be screened and handled?

1. **SCREENING QUESTIONNAIRE:** All individuals presenting to the OPD or ER entrance should be screened with the following questions:

a. Symptoms:

Do you have any of the following symptoms?

- Cough? Fever? Shortness of breath? (common)
- Sore throat, headache or body ache? (less common)

b. Travel history or contact with traveler:

Have you

- Recently returned from travel in, or been living in, an affected area in the past 2 weeks?
- Been in close contact in the past 2 weeks with someone returning from travel in an affected area?

c. Exposures:

Did you have any exposures to any of the following?

- Close contact with anyone with fever or respiratory illness of unknown cause

- Known or suspected COVID-positive contact

2. TEMPERATURE: All persons presenting to the OPD or ER should be screened with thermometer on the temple of head following non-contact method.
(If not a no-touch thermometer, it should be cleaned with 60-70% alcohol or an alcohol swab.)

III.C. Case Definitions

The criteria for treating someone as a suspected case is subject to change depending on the dynamics of the epidemic and prevalence of cases inside and outside the country. Adapted from the most recent World Health Organization (WHO) criteria, with modifications, case definitions for COVID-19 *for clinical purposes at hospitals* will be as follows:

Suspected case

A. A patient with acute respiratory illness (fever and at least one sign/symptom of respiratory disease, e.g., cough, shortness of breath), AND a history of travel to or residence in a location reporting community transmission of COVID-19 disease during the 14 days prior to symptom onset;

OR

B. A patient with any acute respiratory illness AND having been in contact with a confirmed or probable COVID-19 case in the last 14 days prior to symptom onset; (see definition of contact below)

OR

C. A patient with severe acute respiratory illness (fever and at least one sign/symptom of respiratory disease, e.g., cough, shortness of breath; AND requiring hospitalization) AND in the absence of an alternative diagnosis that fully explains the clinical presentation.

OR

D. A healthcare worker who provides direct care to patients and has developed fever OR cough OR shortness of breath

OR

E. A patient with fever OR sign/symptom of acute respiratory disease (e.g., cough, shortness of breath) without another explanation of symptoms will be considered as a lower probability suspected case in the absence of an alternative diagnosis, given evidence of global spread of the disease and identification of new cases of COVID-19 within the country.

Probable case

A. A suspected case for whom testing for the COVID-19 virus is inconclusive.

OR

B. A suspected case for whom testing could not be performed for any reason.

Confirmed case

A person with laboratory confirmation of COVID-19 infection, irrespective of clinical signs and symptoms.

Definition of Contact: A contact is a person who experienced any one of the following exposures during the 2 days before and the 14 days after the onset of symptoms of a probable or confirmed case:

1. Face-to-face contact with a probable or confirmed case within 1 meter and for more than 15 minutes; OR
2. Direct physical contact with a probable or confirmed case; OR
3. Direct care for a patient with probable or confirmed COVID-19 disease without using proper personal protective equipment; OR
4. Other situations as indicated by local risk assessments.

Note: for confirmed asymptomatic cases, the period of contact is measured as the 2 days before through the 14 days after the date on which the sample was taken which led to confirmation.

III.D. How and where will a suspected case be handled and transported?

1. All suspected cases should be given a mask and asked to perform hand hygiene with hand sanitizer, and then escorted by a healthcare worker (HCW) to a separate designated area for isolation of suspect cases.
2. The HCW should be wearing proper PPE (Personal Protective Equipment) such as a surgical mask, gloves, and, if contact is expected, gowns. Gown is not necessary if no contact is needed while driving or escorting the patient.
3. A separate space away from other patients, families and visitors (“Fever/Cough/Influenza-like illness” triage clinic) need to be designated for isolation and evaluation of symptomatic suspected cases. If necessary, a temporary structure such as tents should be erected in a separate area away from the entrance of the emergency department or the outpatient clinics.
4. If there are more than one suspected cases, they should be separated at least by 6 feet distance between them.
5. Standard precautions (hand hygiene and use of gloves as necessary) and droplet precautions (surgical mask, face shield or goggles, gown) need to be strictly implemented in the designated area for isolation.
6. For details of the appropriate use of personal protective equipment and other infection control practices in fever clinics or elsewhere in the hospital, please refer to the NMC Interim Guidance on Infection Prevention and Control Practices when COVID-19 is suspected.

III.E. How will a suspect case be disposed after initial evaluation?

1. Suspected COVID-19 cases with mild symptoms do not require hospital admission *for clinical reasons* unless other underlying risk factors for progression exist, such as DM, immunocompromised patient, cardiovascular disease, chronic respiratory conditions, etc.

2. All suspected patients do need to be kept in isolation to contain virus transmission until the infection is ruled out.
3. **Please note that depending on the public health policy adopted by the government at a particular time, all or some suspected cases of COVID-19 in the broader public health interest, may be required to be admitted to isolation units in hospitals or elsewhere, regardless of the severity of symptoms.**
4. If the patient does not meet criteria for a suspected case for COVID-19, and there is no other reason for the patient to be admitted, they can be discharged from the hospital.
5. Refer to Appendix 1 for initial triage, evaluation and management flow chart.

III.F. What is the definition for stability for suspected case?

1. Oxygen saturation $\geq 94\%$ or as appropriate for the altitude of the area in context
2. No extra work of breathing (as visible by tachypnea, use of accessory muscles of respiration)
3. Hemodynamically stable (BP within acceptable ranges, for example SBP >100 ; HR <110 , or, in febrile patients, tachycardia not more than 10/min for each $^{\circ}\text{C}$ rise in temperature)

IV. DIAGNOSIS

IV.A. Who should get tested for SARS CoV-2?

Based on availability of resources, the following criteria will be used to prioritize testing for suspected cases for COVID-19. (See Appendix 1 for algorithm)

- **If resources are available, all suspected cases should be tested for COVID-19 in addition to other respiratory viruses such as influenza**
- **In the absence of adequate testing resources, suspected cases can be tested in the following order of testing priorities:**
 1. Highest Priority group:
 - Hospitalized patients
 - Healthcare workers with symptoms
 - Symptomatic elderly ≥ 60 years of age
 - Symptomatic individuals with underlying chronic conditions, such as diabetes mellitus, heart disease, lung disease, kidney disease or immunocompromised
 - Symptomatic pregnant women
 2. Second Priority group:
 - Individuals with symptoms of fever and cough or shortness of breath, but without history of exposure to suspected or confirmed COVID-19 cases or history of travel to areas affected by COVID-19.
- **Please note that the testing criteria can be expanded by the public health authorities depending on the dynamics of the epidemic and available testing capacity nationally or locally, to include, for example, asymptomatic individuals with history of travel to affected areas or history of contact with confirmed or probable cases.**

IV.B. What type of diagnostic tests will be performed for suspected cases?

1. ALL SUSPECTED CASES:

- Collect upper respiratory tract specimen, preferably nasopharyngeal swab rather than oropharyngeal swab, or both nasopharyngeal and oropharyngeal swabs, for RT-PCR.
- Place the swab in VTM (Viral Transport Medium), making sure the cold chain is maintained with desired temperature 2-8 °C. Do NOT freeze. Do NOT send at room temperature.
- **If initial testing is negative but the suspicion for COVID-19 remains, resampling and testing from multiple respiratory tract sites should be performed.** Infection control precautions for COVID-19 should continue while repeat evaluation is being performed.
- When a validated serological rapid diagnostic test (RDT) for SARS CoV-2 (IgM and IgG test, or Antigen test) becomes available, it can be used as initial screening test for all suspected cases, especially if it is at 6-7 days or more after symptom-onset. Those with positive RDT for IgM should be evaluated with RT-PCR for COVID-19.
- For safety reasons, specimens from a patient with suspected or documented COVID-19 should not be submitted for viral culture

2. HOSPITALIZED PATIENTS:

- Collect specimens from the upper respiratory tract (ideally both nasopharyngeal and oropharyngeal)
- If upper respiratory specimens are negative and clinical suspicion remains, collect specimens from the lower respiratory tract when readily available (expectorated sputum, endotracheal aspirate, or bronchoalveolar lavage in ventilated patient) for COVID-19 virus testing by RT-PCR and bacterial stains/cultures.
- Collect blood cultures for bacteria that cause pneumonia and sepsis, ideally before antimicrobial therapy. DO NOT delay antimicrobial therapy to collect blood cultures.
- In hospitalized patients with confirmed COVID-19, repeated URT and LRT samples can be collected to demonstrate viral clearance. The frequency of specimen collection will depend on local epidemic characteristics and resources.
- For hospital discharge, in a clinically recovered patient, two negative tests, at least 24 hours apart, is recommended.

IV.C. How will the specimens be collected and transported?

- Use appropriate PPE for specimen collection including droplet and contact precautions for upper respiratory specimens (nasopharyngeal and oropharyngeal). Do not sample the nostrils or tonsils.
- Follow airborne precautions for lower respiratory tract specimens (PPE, eye shield, gloves & N-95) in a negative pressure isolation room similar to TB isolation room (See Figure-3)
- When collecting upper respiratory samples, use viral swabs (sterile Dacron or rayon, not cotton) and viral transport media.

- In a patient with suspected COVID-19, especially with pneumonia or severe illness, a single upper respiratory sample does not exclude the diagnosis, and additional URT (upper respiratory tract) and LRT (lower respiratory tract) samples are recommended. Lower respiratory tract samples are more likely to be positive and for a longer period.
- Avoid sputum induction to minimize risk of aerosol transmission.

IV.D. What type of imaging study should be offered initially?

- Chest X-ray should be done in all hospitalized patient with fever and cough or shortness of breath- glass ground opacities and patchy infiltrates are common findings in patients infected with COVID-19
- Chest X-ray should also be offered to the non-hospitalized patients whose respiratory symptoms are worsening
- CT scan of the chest can be performed in patients suspected of COVID-19; however, CT scan is unlikely to give further useful information. CT should only be done in patients with worsening condition at the discretion of the clinicians and availability.

IV.E. What other routine tests should be ordered initially?

1. All hospitalized patients

- complete blood count and differential count (CBC/Diff)
 - Leukopenia and lymphopenia are expected in 85% of COVID-19 patients
- renal function and electrolyte tests to assess kidney injury
- liver function tests
 - Patients may have increased ALT/AST & Bilirubin
- Where available, tests can be sent for D-dimer level, lactate dehydrogenase level, quantitative C-reactive protein, troponin, ferritin, etc.
- Hospitalized patients should get blood, sputum, urine cultures before starting antibiotics

2. Other tests based on availability and indications may include:

- Other causes of fever based on epidemiology and clinical features including typhoid, TB, and tropical diseases such as scrub typhus, dengue, leptospirosis, malaria, kala-azar, etc as per the discretion of the clinician.

V. TREATMENT

V.A. How will the severity of illness be classified?

Severity of illness for patients with COVID-19 are generally classified into the following categories based on WHO Interim Clinical Guidance as shown in Appendix 2.

1. Mild illness
2. Pneumonia
3. Severe pneumonia
4. ARDS
5. Sepsis
6. Septic shock

V.B. Who is at high risk of developing severe illness?

Patients diagnosed with COVID-19 who are at high risk for poor outcomes, including ARDS and death, are those who meet any 1 of the following criteria:

- Age ≥ 60 years
- Any 1 of the following medical conditions:
 - Cardiovascular disease, excluding hypertension as the sole cardiovascular diagnosis
 - Diabetes with HbA1c level $>7.5\%$
- Chronic pulmonary diseases, including asthma
 - End-stage renal disease
 - Advanced liver disease
 - Blood disorders (e.g., sickle cell disease)
 - Neurologic or neurodevelopmental disorders
 - Post–solid organ transplantation, on immunosuppressive therapy
 - Use of biologic agents for immunosuppression
 - Undergoing treatment with chemotherapy or immunotherapies for malignancy
 - Within 1 year post–marrow transplant
 - Undergoing treatment for graft-versus-host disease
 - HIV infection, with CD4 cell count <200 copies/ mm^3
- Any one of the following clinical findings:
 - Oxygen saturation (SaO₂) $\leq 93\%$ on room air; $<90\%$ if known chronic hypoxic conditions or receiving chronic supplemental oxygen
 - Respiratory rate >24 breaths/min
- Laboratory finding: D-dimer level >1 $\mu\text{g/mL}$ in patients with respiratory illness

Note: Other lab findings such as elevated lactate dehydrogenase, elevated prothrombin time, elevated troponin, etc. have also been associated with worse outcomes.

V. C. How will mild COVID-19 be managed?

- Patients with mild COVID-19 infection do not require hospital admission *for clinical reasons* unless other underlying risk factors for progression exist, such as DM, immunocompromised patient, cardiovascular disease, chronic respiratory conditions, etc.
- Patients need to be kept in isolation to contain virus transmission.
- **Please note that depending on the public health policy adopted by the government at a particular time, hospitals may be required, in the broader public health interest, to admit individuals with mild COVID-19 to isolation unit.** Otherwise they can be discharged to home or a designated isolation unit elsewhere with instructions regarding “self-isolation“, after notifying the appropriate public health officials about the discharge.

- If the patient is discharged to isolation at home or another designated location, they should be counseled about signs and symptoms of progression and if they develop any of these symptoms, they should return to designated hospital immediately.
- Use symptomatic treatment such as antipyretics (preferably acetaminophen) for fever
- Avoid nebulization, if possible, or use dry nebulization protocol (See Appendix 4) as a non-aerosol generating option.

V.D How will severe COVID-19 including pneumonia be managed?

1. Severe COVID-19 criteria (any one of the following):
 - Respiratory rate ≥ 30 breaths/min
 - $SPO_2 \leq 93\%$ in room air at rest
 - $PaO_2/FiO_2 \leq 300$ mmHg or SF ratio ≤ 315 (use SF ratio = SpO_2/FiO_2 if ABG not available)
2. Indications for ICU admission (any one of the following):
 - Respiratory failure requiring mechanical ventilation
 - Presence of shock
 - Older patients (>60 years) with comorbidities and any one of the severity criteria above
 - $PaO_2/FiO_2 < 200$ mmHg or SF ratio ≤ 235 if ABG not available with respiratory distress
3. Oxygen Therapy and Monitoring:
 - Monitor oxygen saturation continually during oxygen therapy
 - Give supplemental oxygen therapy immediately to patients with severe acute respiratory infection (SARI) and respiratory distress, hypoxemia or shock.
 - Target oxygen saturation:
 - 93% - 96% for patients without chronic respiratory disease
 - 88% - 92% for patients with chronic type II respiratory failure
 - Endotracheal intubation:
 - If worsening respiratory distress with $SPO_2 < 90\%$ despite oxygen supplementation with 10-15 litres/minute via non-rebreathing facemask, and
 - $PaO_2/FiO_2 < 150$ mmHg
4. Mechanical ventilation:
 - If patients have indications for mechanical ventilation, intubate them without delay with airborne precautions. Use rapid sequence intubation (preoxygenation, sedation, neuromuscular blocking (NMB) agents, intubation) technique to minimize bag-mask ventilation and to minimize aerosol generation
 - Non-invasive ventilation (NIV) or high flow nasal cannula (HFNC) are not preferred because of concerns with aerosol generation and may have worse outcome compared to invasive ventilation by delaying intubation.
They may only be considered in COVID-19 patients when there is shortage of ventilators.

- In case of severe crisis and ventilator shortages in the country, anesthesia workstations can be used for ventilation of patients with COVID-19.
- 5. Airway management: Full airborne precautions measures should be adopted when performing Bag and Mask Ventilation or endotracheal intubation or any other aerosol generating procedures. Viral filters should be used when available. (Refer to NMC Interim Guidance for Infection Prevention and Control When COVID-19 is Suspected 2020)
- 6. Treatment of co-infections: At initial presentation, if bacterial pneumonia or sepsis is suspected, start empiric antimicrobials to treat likely pathogens causing severe pneumonia and sepsis as soon as possible, preferably within 1 hour of initial assessment for patients with sepsis. If bacterial pathogens are unlikely or ruled out and a viral pathogen such as COVID-19 has been identified, antibiotics should be avoided.
 - a. Example of empiric antibiotic regimen: Ceftriaxone or Amoxicillin-clavulanic acid
 - b. Add Azithromycin for atypical coverage of pneumonia; substitute with Doxycycline if allergic to macrolides or if hydroxychloroquine is initiated.
 - c. Add Oseltamivir if influenza cannot be ruled out or test is positive.
 - d. **When a viral etiology such as coronavirus is identified, empiric antibiotic therapy should be deescalated or stopped on the basis of microbiology results and clinical judgement.**
- 7. Closely monitor patients for signs of clinical deterioration, such as rapidly progressive respiratory failure and sepsis
- 8. Fluid management:
 - Use restrictive fluid management strategy ensuring patient's tissue perfusion.
 - In patients with severe acute respiratory illness, when there is no evidence of shock, aggressive fluid management may worsen oxygenation.
 - Closely monitor fluid intake and output.
- 9. DVT prophylaxis:
 - Start pharmacologic DVT prophylaxis if no contraindication.

V.E. How will ARDS secondary to COVID-19 be managed?

- (Refer to Appendix 5 for management of refractory hypoxemia and ventilator adjustment.)
1. Recognize severe hypoxemic respiratory failure and prepare to provide advanced oxygen/ventilatory support when a patient has worsening respiratory distress and is failing to respond to standard oxygen therapy ($\text{PaO}_2/\text{FiO}_2 < 150$ mmHg).
 2. Endotracheal intubation should be performed by a trained and experienced provider using airborne precautions and using full PPE.
 3. Implement mechanical ventilation using lower tidal volumes (4–8 mL/kg predicted body weight, PBW) and lower inspiratory pressures (plateau pressure < 30 cmH₂O)
 4. Proning:
 - a. Early proning without pulmonary vasodilator trial is recommended in adult patients with severe ARDS due to COVID-19, which is a departure from the typical practice for ARDS from other causes. In adult patients with severe ARDS ($\text{PaO}_2/\text{FiO}_2$ less than 150 mmHg), prone early, within 12 hours of $\text{FiO}_2 > 75\%$, for 12–16 hours per day.

- b. Spinal cord injury and open chest are absolute contraindications to prone ventilation.
- c. Prone positioning may be associated with several complications; hence, experienced team should carry out or supervise the management of prone patients. Several sessions of prone positioning may be needed.
5. Titrate PEEP and FiO₂ as per ARDSnet's protocol. (Appendix 5)
6. Adopt Permissive hypercapnia (Target pH > 7.2)
7. Use a conservative fluid management strategy for ARDS patients without tissue hypoperfusion.
8. Use in-line catheters (Closed Suction Catheter) for airway suctioning, and clamp endotracheal tube when disconnection is required. Consider paralysis during airway manipulation.
9. Use Ventilator Bundle strictly. (Appendix 6)
10. Sedation and neuromuscular blockade: Avoid continuous sedation and neuromuscular blockade when possible. Sedation should be given in case of ventilator dyssynchrony. Intermittent boluses of neuromuscular blocking agents can be given if there are some ventilator dyssynchrony. If persistent dyssynchrony, high plateau pressures or if prone ventilation then continuous NMBA may be need for upto 48 hrs.
11. In children, a lower level of plateau pressure (< 28 cmH₂O) is targeted, and lower target of pH is permitted (7.15–7.30). Tidal volumes should be adapted to disease severity: 3–6 mL/kg PBW in the case of poor respiratory system compliance, and 5–8 mL/kg PBW with better preserved compliance. Early proning for extended duration (24-48 hours) may be needed in children. Use restrictive fluid strategy. Aim for euolemia. If signs of volume overload are present consider diuresis with furosemide. Strict intake and output with foley catheter monitoring is recommended.

V.F. How will Septic Shock secondary to COVID-19 be managed?

1. Recognition of septic shock

- a. Recognize septic shock in adults when infection is suspected or confirmed AND vasopressors are needed to maintain mean arterial pressure (MAP) \geq 65 mmHg AND lactate is \geq 2 mmol/L, in absence of hypovolemia. If lactate measurement is not available use clinical assessment for tissue perfusion status e.g. capillary refill time, change in mental status, urine output.
- b. Recognize septic shock in children with any hypotension (systolic blood pressure [SBP] < 5th centile or > 2 SD below normal for age) or two or more of the following: altered mental state; bradycardia or tachycardia (HR < 90 bpm or > 160 bpm in infants and HR < 70 bpm or > 150 bpm in children); prolonged capillary refill (> 2 sec) or feeble pulses; tachypnea; mottled or cold skin or petechial or purpuric rash; increased lactate; oliguria; hyperthermia or hypothermia.

2. Resuscitation of patients with septic shock

- a. Adults: give 500 mL crystalloid fluid (such as Normal saline or Ringer's lactate) as rapid bolus in first 15 minutes and reassess for signs of fluid overload after each bolus.
- b. Children: give 10–20 mL/kg crystalloid fluid as a bolus in the first 30 minutes and reassess for signs of fluid after each bolus.

- c. Fluid resuscitation may lead to volume overload and respiratory failure, particularly with ARDS. If there is no response to fluids or if patient develops signs of volume overload (e.g. jugular venous distension, crackles on lung auscultation, pulmonary oedema on imaging, B lines on Lung USG, or hepatomegaly in children), then reduce or discontinue fluid administration.
- d. Do not use hypotonic crystalloids, starches, or gelatins for resuscitation.

3. Vasopressors

- a. Adults: administer vasopressors when shock persists during or after fluid resuscitation. The initial blood pressure target is MAP \geq 65 mmHg in adults and improvement in markers of perfusion.
 - Norepinephrine is considered first-line treatment in adult patients; vasopressin and /or epinephrine 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.
- b. Children: administer vasopressors if
 - i. Signs of shock such as altered mental state; bradycardia or tachycardia (HR < 90 bpm or > 160 bpm in infants and H R < 70 bpm or > 150 bpm in children); prolonged capillary refill (> 2 seconds) or feeble pulses; tachypnea; mottled or cool skin or petechial or purpuric rash; increased lactate; oliguria persists after two repeat boluses; or
 - ii. age-appropriate blood pressure targets are not achieved; or
 - iii. signs of fluid overload are apparent
 - In children, Epinephrine is considered first-line treatment, while Norepinephrine can be added if shock persists despite optimal dose of epinephrine.
- c. Vasopressors (i.e. norepinephrine, vasopressin, epinephrine and dopamine) are most safely given through a central venous catheter at a strictly controlled rate, but it is also possible to safely administer them via peripheral vein (lower concentration solution) and intraosseous needle.
- d. Monitor blood pressure frequently and titrate the vasopressor to the minimum dose necessary to maintain perfusion targeting MAP of 60-65 mmHg and also prevent side effects.

4. Antibiotics:

- a. The rates of bacterial superinfection of COVID-19 appear to be low (10-20%), but when present increase mortality risk. Anecdotal reports suggest less MRSA superinfection than is often seen with influenza. **Unnecessary antibiotics carry risks of fluid overload and drug-resistance, as well as the possibility that antibiotics may become a limited resource.**
- b. In patients who meet the definition of sepsis/septic shock, antibiotics should be started within an hour of presentation or recognition of signs of sepsis. The initial antibiotic regimens should be chosen based on the type of patients.

- c. For empiric coverage of a presumed pulmonary source of infection.
In patients **without** risk factors for MRSA or *Pseudomonas* (i.e., community acquired infection, no prior multi-drug resistant organisms): Ceftriaxone or Amoxicillin-clavulanic acid +/- Azithromycin or doxycycline
(If the patient is getting treatment with chloroquine or hydroxychloroquine, doxycycline should be preferred to azithromycin to avoid QTc prolongation.)
In patients **with** risk factors for *Pseudomonas* or MRSA (i.e., hospital-acquired infection, recent courses of antibiotics): Cefepime or Piperacillin/tazo +/- Teicoplanin or Vancomycin.
Consider adding Meropenem or Imipenem-cilastatin if high concern for multidrug resistant organism infection.
- d. Give oral antibiotics when possible to reduce volume load, unless concerns for poor oral absorption.
- e. **Antibiotics should be discontinued or deescalated if cultures are reported as negative or if bacterial infection ruled out clinically.**
- f. Coverage of potential coinfections:
 - If concurrent influenza, treat with oseltamivir.
 - Given prevalence of lymphopenia in clinical presentation of COVID-19, consider *Pneumocystis* and treat accordingly.

V.G. How will pregnant and lactating mothers be managed?

1. Based on currently available information, there is no evidence that pregnant women are at higher risk or at risk of severe illness.
2. So far, there is little evidence of mother-to-child transmission when infection occurs in the third trimester.
3. SARS-CoV-2 has not been identified in breastmilk of infected mothers.
4. All recently pregnant women with COVID-19 should be counseled on safe infant feeding and appropriate infection prevention measures to prevent COVID-19 virus transmission.
5. Infants born to mothers with suspected, probable, or confirmed COVID-19 should be fed according to standard infant feeding guidelines, while applying necessary precautions for infection prevention and control
6. Symptomatic mothers who are breastfeeding or practicing skin-to-skin contact or kangaroo mother care should practice respiratory hygiene, including during feeding (for example, use of a medical mask when near a child if with respiratory symptoms), perform hand hygiene before and after contact with the child, and routinely clean and disinfect surfaces which the symptomatic mother has been in contact with.

V.H. What antiviral or other COVID-19 specific treatment should be offered to COVID-19 patients?

1. **There is no currently proven antiviral medication for COVID-19. These therapeutic strategies are based on collective clinical experiences and anecdotal usage in other countries dealing**

with the epidemic. These drugs should be used only in consultation with experts, whenever possible.

2. The following drugs have been used as antiviral medications during current outbreak:
 - a. Hydroxychloroquine/Chloroquine: These are potentially effective against SARS and COVID-19 and are thought to work by interfering with cellular receptor ACE2 and affecting viral cell entry. They are also thought to blunt the excessive inflammatory response which may result in ARDS. So far, a very small French study of hydroxychloroquine with or without azithromycin and several non-randomized studies from China assessing the efficacy of chloroquine in COVID-19 patients have suggested potential use of these medications in COVID-19 patients, however there were severe limitations of those studies making it difficult to make recommendations for COVID-19 patients at this point in general. Several clinical trials are ongoing to assess their roles in treatment of COVID-19 and in prophylaxis in at risk population. At this point, given the inavailability of effective pharmaceutical interventions against COVID-19, the known in vitro activity of these drugs against SARS-CoV-2 and relative safety of short term use of hydroxychloroquine or chloroquine, clinicians are using these medications mostly in hospitalized COVID-19 patients with severe infections or those at risk of developing severe complications, especially if those patients do not qualify for clinical trials with other medications.
 - b. Chloroquine, hydroxychloroquine and azithromycin are associated with QT-prolongation and caution has been advised in using them.
 - c. Remdesivir: It is a nucleotide analog that blocks RNA polymerase. It has shown some activity against MERS and clinical trials are ongoing in multiple countries to assess its efficacy against SARS-CoV-2. It could be considered for treatment of COVID-19 in Nepal if it could be obtained under “compassionate use” from Gilead. It is under clinical trial for COVID-19 in multiple countries and further data is awaited.
 - d. Lopinavir/Ritonavir (Kaletra) and other HIV protease inhibitors: These medications cannot be recommended at this point for treatment of COVID-19. Recent publications showed no difference in patients who received Lopinavir/Ritonavir compared to those who did not.
 - e. Favipiravir: It is a purine nucleoside that acts as a competitive inhibitor of viral RNA-dependent RNA polymerase, and previously was approved for influenza in Japan. An open label prospective randomized trial has been reported (still in preprint) showing superior clinical improvement and recovery rate compared to Umifenovir in those with moderate COVID-19 but not in those with severe COVID-19. However, a placebo control group was not included. The data on the efficacy and safety of Favipiravir is still very limited for this to be recommended in most patients with COVID-19.

- f. Umifenovir: Sold under the brand name Arbidol, Umifenovir is another antiviral used in China and Russia for influenza. It has been used to treat COVID-19 infections and is under clinical trials in China, but its efficacy and safety remain unclear.
3. The following agents have been used as immunomodulatory drugs in COVID-19; however, experience is limited for their use and should be used only in consultation with experts.
- a. Tocilizumab: It is a monoclonal antibody (mAb) to IL-6 receptor that inhibits inflammatory response. It has been used as an immunomodulatory agent for COVID-19 patients with sepsis syndrome to block high IL-6 and cytokine storm. Small case series have reported potentially promising data, but other trials are ongoing. It needs to be avoided in patients with other infections.
 - b. Convalescent plasma: A preliminary, uncontrolled case series of patients receiving convalescent plasma with neutralizing antibody showed some improvement in clinical status. Further studies are expected to give more reliable information about the efficacy of this potentially promising treatment for COVID-19.
 - c. Nebulized alpha interferon: There has been no proven benefit however studies are ongoing.
4. **Based on currently available treatment experience in other countries, the following antiviral and immunomodulatory treatment can be considered in appropriate patients under close clinical monitoring.**
- a. **Hydroxychloroquine or Chloroquine:**
 - a) Based on availability, Hydroxychloroquine or Chloroquine can be used as the antiviral option for immediate use for:
 - i. Patients who meet any one of the criteria for risk of severe illness or poor outcomes including ARDS or even death.(listed above in section V.B)
 - ii. Any inpatient who, while hospitalized, develops any one of the medical conditions or clinical findings listed in section V.B
 - b) Because of better safety profile and some evidence of slightly better antiviral activity, hydroxychloroquine is preferred to chloroquine if available.
 - c) Dose:
 - Hydroxychloroquine 400 mg po 12 hourly for 2 doses on first day, then 24 hourly for 4 more days
 - Chloroquine 1000 mg on first day, then 500 mg 24 hourly for 4 more days
 - c) Check ECG to assess QT interval before starting chloroquine or hydroxychloroquine.
 - d) Contraindication for Hydroxychloroquine: decompensated heart failure, QTc> 500, known or suspected G6PD deficiency.
 - e) Watch for drug interactions especially with drugs with hepatic metabolism.

b. If/when available, and depending on further information from ongoing clinical trial data, the following may be considered as for treatment for COVID-19. It is anticipated that these guidelines will be updated as more evidence emerges regarding treatment with these agents.

- a) Remdesivir
- b) Tocilizumab
- c) Convalescent plasma

5. Prophylaxis with Chloroquine or Hydroxychloroquine for healthcare workers is NOT supported by clinical evidence as of now. It is being studied in clinical trials. It cannot be recommended at this stage secondary to potential harms.

V.I. What other adjunct treatment considerations are there?

- Systemic corticosteroids: Use of systemic corticosteroids for treatment of viral pneumonia is not recommended, unless absolutely required for adrenal crisis or comorbidities such as COPD or asthma exacerbation.
- Antimicrobials:
 - Discontinue antibiotics if COVID-19 positive and there is no sign of secondary bacterial infections.
 - Oseltamivir can be discontinued if influenza PCR test is negative
- Antihypertensive medications: Patients on anti-hypertensive medication should continue to take ACEI/ARB and should be stopped only when they develop hypotension. Switching to other group of antihypertensives is not recommended. SARS CoV-2 uses ACE-2 receptors and effect of these drugs in COVID-19 is unknown.
- Management of myocarditis: Patients may develop cardiogenic shock secondary to myocarditis, in which case check ECG and trends of BNP and troponin. Refer these patients to cardiologist for appropriate management.
- Nonsteroidal anti-inflammatory drugs: Although concern was raised earlier regarding the potential negative impact of NSAIDs in COVID-19 outcomes, this was only based on a few anecdotal reports. There is no clear evidence to recommend stopping or avoiding NSAIDs when clinically indicated. However, given the uncertainty, it is advised to use Paracetamol as the preferred temperature-lowering agent and analgesic, and when NSAIDs are needed, to use the lowest effective dose.
- Nutritional Support:
 - Start enteral feeding early.
 - Nasogastric or orogastric tube feeding in intubated patients
 - Consider parenteral nutrition if enteral feeding is not tolerated despite prokinetics use or if enteral feeding is contraindicated.
- DVT prophylaxis: All critically ill patients should be given DVT prophylaxis unless contraindicated. One of the following may be used: Enoxaparin, Dalteparin, Fondaparinux or Unfractionated Heparin.

- Extracorporeal membrane oxygenation (ECMO) therapy:
 - Consider ECMO if resources are available, in patients with refractory hypoxemia in spite of management including lung protective mechanical ventilation and prone positioning.

V.J. What possible ethical issues need to be considered?

1. End-of-life care and care of the dying patient

- a. Patients who are terminal because of COVID–19 may be allowed to be visited by only a limited number closest family members at their wish but with appropriate PPE. If appropriate PPE is not available, hospitals may refuse such visits considering the risk of transmission of the virus.
- b. If the patient’s outcome seems grim and the treatment offered may be futile as evidenced by multiple organ failures, refractory shock or refractory hypoxia, this should be conveyed to family members and opted for a DNR status as providing CPR to the patient won’t be helpful and will increase the risk of transmission of disease.

2. Resource utilization during crisis

- a. In case of rapid significant increase in the number of cases requiring critical care and mechanical ventilation beyond the effectively available critical care capacity, such increase may give rise to a situation when criteria for access to (and discharge from) intensive care resources and ventilators may need to be set up, based not only on clinical appropriateness and proportionality of care, but also on likelihood of therapeutic success, while also aspiring towards distributive justice. Principles of justice, transparency, non-abandonment of patient, and, non-restriction of autonomy of the patient except for compelling public health concern, should be followed while designing such criteria.
- b. Parameters indicating likelihood of therapeutic success may include:
 - i. the type and severity of the disease
 - ii. the compromise of other organ systems and their reversibility
 - iii. the presence of hypoxic brain Injury
 - iv. types, numbers and severity of underlying comorbidities
 - v. age
- c. Such decisions regarding withholding access to intensive care unit interventions or withdrawing of active life sustaining treatment of patients (including mechanical ventilation) need to be made by a separate team or committee formed by the hospital (Ethics Committee, Triage Committee, or a similar entity) with at least three members (as stipulated in the Nepal Medical Council Guidelines “Professional Ethics During COVID-19 Pandemic”). Treating clinical team members should not be a part of this committee. The Ethics Committee’s decision has to be documented in writing and signed by all members.
- d. Communication about such decisions should be done to the patient’s family or concerned parties by the Ethical Committee members and not by the treating critical care team.

3. Prioritization of resources to healthcare workers:

- a. Critical Covid-19 interventions such as lab tests, personal protective equipment, intensive care unit interventions such as ventilators, therapeutics, and vaccines should preferentially be made available to front-line health care workers and others who care for ill patients and who keep critical infrastructure operating, particularly those who face a high risk of infection.
 - i. Whether healthcare workers who need ventilators will be able to return to work is uncertain, but providing preferential access to appropriate interventions as indicated recognizes the significant risks they have willingly exposed themselves to while taking care of suspected or confirmed COVID-19 patients.

V.K. What are the criteria for discharge of confirmed COVID-19 patients?

1. Criteria for discharge from the ICU

- a. Hemodynamically Stable (No support required) > 8 hours
- b. Off Ventilators > 24 hours

2. Criteria for discharge to home

- a. Consider discharging patients who meet both clinical and laboratory criteria as follows. However, in the absence of access to lab testing, all clinical criteria should be met and patients must continue home isolation for 2 additional weeks.
 - i. Clinical criteria:
 - a) Resolution of fever >72 hours without antipyretics, and
 - b) Improvement in respiratory signs and symptoms (cough, shortness of breath and oxygen requirement), and
 - c) At least 7 days have passed since the initial onset of symptoms
 - ii. Laboratory criteria:
 - a) Negative results for COVID-19 nucleic acid (PCR) testing from at least 2 respiratory tract specimens collected \geq 24 hours apart

3. Home Isolation:

- a. Patients must continue 2 weeks of isolation at home after discharge.
- b. They should be provided with a surgical mask as available at the time of discharge and instructed about appropriate precautions to be taken at home.

VI. INFECTION PREVENTION AND CONTROL

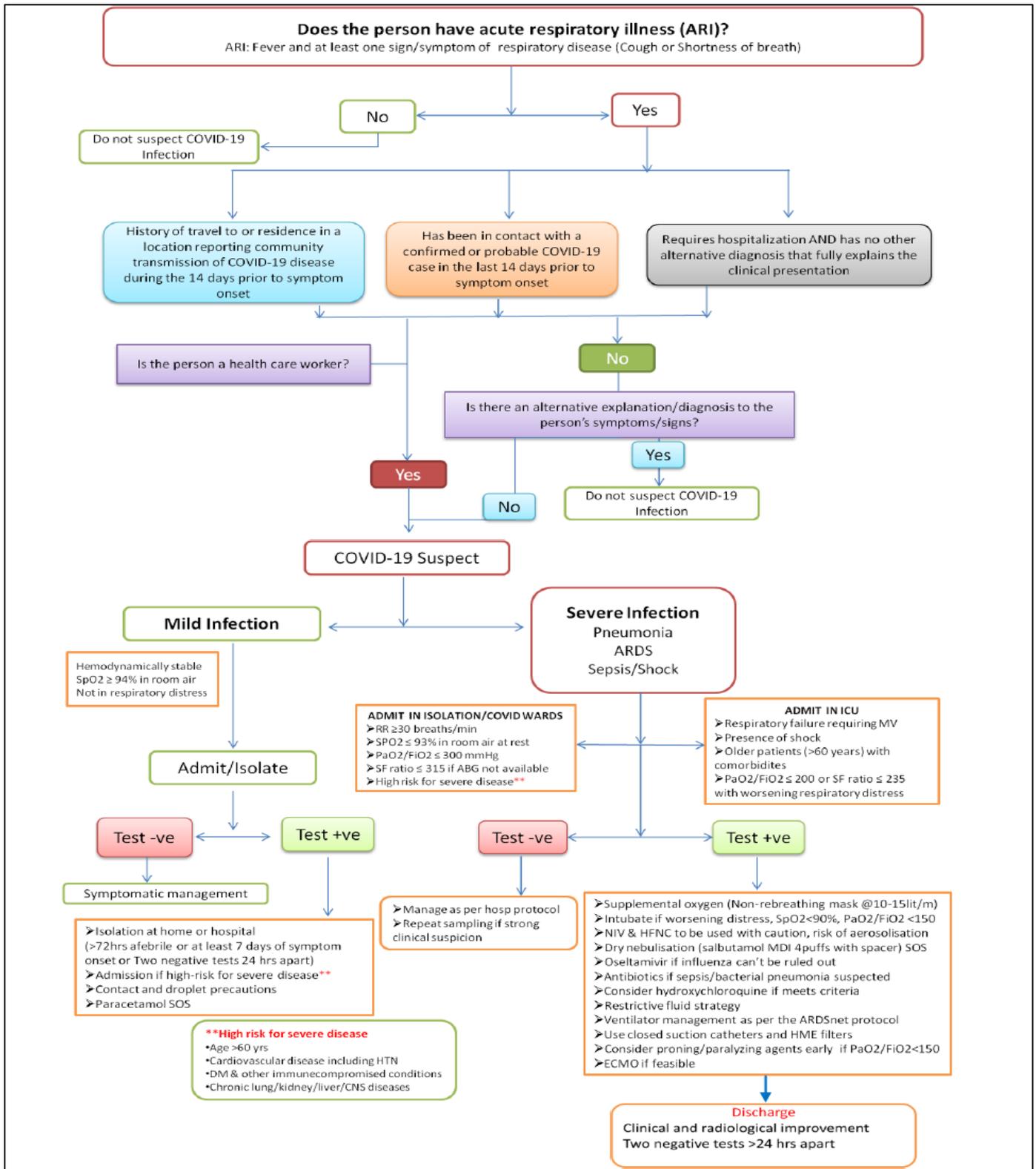
Please refer to the separately published *Nepal Medical Council Interim Guidance for Infection Prevention and Control When COVID-19 Is Suspected* for guidance regarding infection prevention and control in hospitals.

VII. REFERENCES

- Operational Planning Guidelines to Support Country Preparedness and Response. WHO, Feb 2020.
- Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected: Interim guidance. WHO March 2020.
- Global surveillance for COVID-19 caused by human infection with COVID-19 virus: interim guidance WHO. March 2020.
- Comparative accuracy of oropharyngeal and nasopharyngeal swabs for diagnosis of COVID-19. Oxford COVID-19 Evidence Service Team, Centre for Evidence-Based Medicine, Nuffield Department of Primary Care Health Sciences, University of Oxford. March 26, 2020. <https://www.cebm.net/covid-19/comparative-accuracy-of-oropharyngeal-and-nasopharyngeal-swabs-for-diagnosis-of-covid-19/>
- Profiling Early Humoral Response to Diagnose Novel Coronavirus Disease (COVID-19) Guo et al. ClinInf Dis. <https://doi.org/10.1093/cid/ciaa310>
- Brigham and Women's Hospital COVID-19 Critical Care Clinical Guidelines. www.covidprotocols.org Accessed March 31, 2020.
- King's Critical Care – Evidence Summary: Clinical Management of COVID-19. King's College Hospital NHS Foundation Trust, 2020.
- Intensive Care Management of COVID-19 by Ithan Peltan, MD, MSc and Eliotte Hirshberg, MD, Intermountain Healthcare. Updated March 13, 2020.
- Favipiravir versus Arbidol for COVID-19: a randomized clinical trial. BMJ. Chen et al. doi: <https://doi.org/10.1101/2020.03.17.20037432>
- SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients. N Engl J Med. Zou et al. PMID: 32074444 DOI: 10.1056/NEJMc2001737
- Prone Positioning in Severe Acute Respiratory Distress Syndrome. N Engl J Med. Guerin et al. PMID: 23688302. DOI: [10.1056/NEJMoa214103](https://doi.org/10.1056/NEJMoa214103)
- Using RAAS Antagonists in COVID-19. HFSA/ACC/AHA. 2020. <https://www.acc.org/latest-in-cardiology/articles/2020/03/17/08/59/hfsa-acc-aha-statement-addresses-concerns-re-using-raas-antagonists-in-covid-19>. Accessed March 30, 2020
- [Surviving Sepsis Campaign: Guidelines on the Management of Critically Ill Adults with Coronavirus Disease 2019 \(COVID-19\)](https://www.sccm.org/2020/03/20/surviving-sepsis-campaign-guidelines-on-the-management-of-critically-ill-adults-with-coronavirus-disease-2019-covid-19) March 20, 2020
- COVID-19 Science Report: Therapeutics. NUS Saw Swee Hock School of Public Health As of March 30, 2020.
- JHMI Clinical Guidance for Available Pharmacologic Therapies for COVID-19. Last updated March 25, 2020. Writing group of the Johns Hopkins University and Johns Hopkins Hospital COVID-19 Treatment Guidance Working Group. https://www.hopkinsguides.com/hopkins/ub?cmd=repview&type=479-1122&name=4_538747_PDF
- Handbook of COVID-19 Prevention and Treatment. The First Affiliated Hospital, Zhejiang University School of Medicine. 2020.
- A Trial of Lopinavir–Ritonavir in Adults Hospitalized with Severe Covid-19. Cao B, et al. NEngJMed March 2020
- Covid-19 - The Search for Effective Therapy. Baden L, et al. NEJM March 2020
- Interim Infection Prevention and Control Guidelines, CDC. March 10, 2020.
- New insights on the antiviral effects of chloroquine against coronavirus: what to expect for COVID-19? Devaux CA, Rolain JM, Colson P, Raoult D. Int J Antimicrob Agents. 2020 Mar 11
- Managing the Respiratory Care of Patients with COVID-19. Italian Thoracic Society. 2020
- Nepal Medical Council. Interim Guidance for Infection Prevention and Control When COVID-19 Is Suspected. April 2020.
- WHO Global surveillance for COVID-19 caused by human infection with COVID-19 virus Interim guidance 20 March 2020.

VIII. APPENDICES:

APPENDIX 1: Patient triage and isolation flow chart



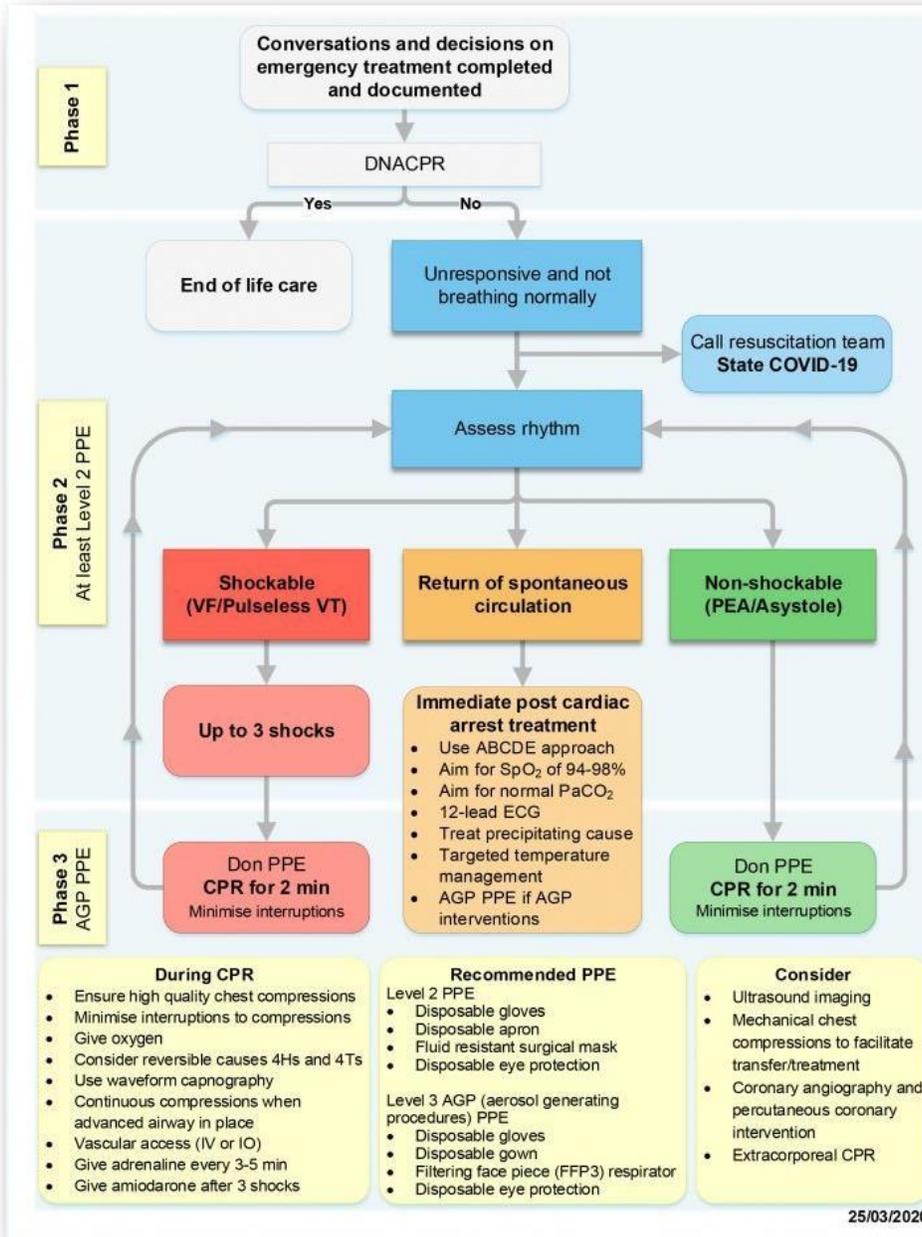
APPENDIX 2: Clinical syndromes associated with COVID-19 (Source- WHO Interim Guidance, March 2020)

Mild illness	<p>Patients uncomplicated upper respiratory tract viral infection may have non-specific symptoms such as fever, fatigue, cough (with or without sputum production), anorexia, malaise, muscle pain, sore throat, dyspnea, nasal congestion, or headache. Rarely, patients may also present with diarrhoea, nausea, and vomiting (3, 11-13).</p> <p>The elderly and immunosuppressed may present with atypical symptoms. Symptoms due to physiologic adaptations of pregnancy or adverse pregnancy events, such as dyspnea, fever, GI-symptoms or fatigue, may overlap with COVID-19 symptoms.</p>
Pneumonia	<p>Adult with pneumonia but no signs of severe pneumonia and no need for supplemental oxygen.</p> <p>Child with non-severe pneumonia who has cough or difficulty breathing + fast breathing: fast breathing (in breaths/min): < 2 months: ≥ 60; 2–11 months: ≥ 50; 1–5 years: ≥ 40, and no signs of severe pneumonia.</p>
Severe pneumonia	<p>Adolescent or adult: fever or suspected respiratory infection, plus one of the following: respiratory rate > 30 breaths/min; severe respiratory distress; or $SpO_2 \leq 93\%$ on room air (adapted from 14).</p> <p>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 a general danger sign: inability to breastfeed or drink, lethargy or unconsciousness, or convulsions (15). Other signs of pneumonia may be present: chest indrawing, fast breathing (in breaths/min): < 2 months: ≥ 60; 2–11 months: ≥ 50; 1–5 years: ≥ 40 (16). While the diagnosis is made on clinical grounds; chest imaging may identify or exclude some pulmonary complications.</p>
Acute respiratory distress syndrome (ARDS) (17-19)	<p>Onset: within 1 week of a known clinical insult or new or worsening respiratory symptoms.</p> <p>Chest imaging (radiograph, CT scan, or lung ultrasound): bilateral opacities, not fully explained by volume overload, lobar or lung collapse, or nodules.</p> <p>Origin of pulmonary infiltrates: respiratory failure not fully explained by cardiac failure or fluid overload. Need objective assessment (e.g. echocardiography) to exclude hydrostatic cause of infiltrates/oedema if no risk factor present.</p> <p>Oxygenation impairment in adults (17, 19):</p> <ul style="list-style-type: none"> • Mild ARDS: $200 \text{ mmHg} < PaO_2/FiO_2^a \leq 300 \text{ mmHg}$ (with PEEP or CPAP $\geq 5 \text{ cmH}_2\text{O}$, or non-ventilated) • Moderate ARDS: $100 \text{ mmHg} < PaO_2/FiO_2 \leq 200 \text{ mmHg}$ (with PEEP $\geq 5 \text{ cmH}_2\text{O}$, or non-ventilated) • Severe ARDS: $PaO_2/FiO_2 \leq 100 \text{ mmHg}$ (with PEEP $\geq 5 \text{ cmH}_2\text{O}$, or non-ventilated) • When PaO_2 is not available, $SpO_2/FiO_2 \leq 315$ suggests ARDS (including in non-ventilated patients). <p>Oxygenation impairment in children: note $OI = \text{Oxygenation Index}$ and $OSI = \text{Oxygenation Index using } SpO_2$. Use PaO_2-based metric when available. If PaO_2 not available, wean FiO_2 to maintain $SpO_2 \leq 97\%$ to calculate OI or SpO_2/FiO_2 ratio:</p> <ul style="list-style-type: none"> • Bilevel (NIV or CPAP) $\geq 5 \text{ cmH}_2\text{O}$ via full face mask: $PaO_2/FiO_2 \leq 300 \text{ mmHg}$ or $SpO_2/FiO_2 \leq 264$ • Mild ARDS (invasively ventilated): $4 \leq OI < 8$ or $5 \leq OSI < 7.5$ • Moderate ARDS (invasively ventilated): $8 \leq OI < 16$ or $7.5 \leq OSI < 12.3$ <p>Severe ARDS (invasively ventilated): $OI \geq 16$ or $OSI \geq 12.3$.</p>
Sepsis (5, 6)	<p>Adults: life-threatening organ dysfunction caused by a dysregulated host response to suspected or proven infection.^b Signs of organ dysfunction include: altered mental status, difficult or fast breathing, low oxygen saturation, reduced urine output (5, 20), fast heart rate, weak pulse, cold extremities or low blood pressure, skin mottling, or laboratory evidence of coagulopathy, thrombocytopenia, acidosis, high lactate, or hyperbilirubinemia.</p> <p>Children: suspected or proven infection and ≥ 2 age- based systemic inflammatory response syndrome criteria, of which one must be abnormal temperature or white blood cell count.</p>
Septic shock (5, 6)	<p>Adults: persisting hypotension despite volume resuscitation, requiring vasopressors to maintain MAP ≥ 65 mmHg and serum lactate level $> 2 \text{ mmol/L}$.</p> <p>Children: any hypotension (SBP < 5th centile or > 2 SD below normal for age) or two or three 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 feeble pulse; tachypnoea; mottled or cool skin or petechial or purpuric rash; increased lactate; oliguria; hyperthermia or hypothermia (21).</p>

^a If altitude is higher than 1000 m, then correction factor should be calculated as follows: $PaO_2/FiO_2 \times \text{barometric pressure}/760$.

^b The SOFA score ranges from 0 to 24 and includes points related to six organ systems: respiratory (hypoxemia defined by low PaO_2/FiO_2); coagulation (low platelets); liver (high bilirubin); cardiovascular (hypotension); central nervous system (low level of consciousness defined by Glasgow Coma Scale); and renal (low urine output or high creatinine). Sepsis is defined by an increase in the sepsis-related SOFA score of ≥ 2 points. Assume the baseline score is 0 if data are not available (22).

APPENDIX 3: Advanced Cardiovascular Life Support Flowchart in Healthcare Settings
(Source: Resuscitation Council, UK)



Key Points

Ensure all members of the resuscitation team have full personal protective equipment (PPE) for aerosol generating procedure before starting BLS and ACLS.

Do not do mouth-to-mouth ventilation or use a pocket mask. Place face mask, preferably non-rebreathing mask, with oxygen on the patient's face during chest compressions to limit aerosol spread during compressions.

Avoid bag and mask ventilation prior to intubation

Airway interventions (e.g. supraglottic airway insertion or tracheal intubation) must be carried out by experienced medical personnel to minimise delay

Any work surfaces and all equipment used for airway/resuscitation need to be cleaned or disposed or disinfected according to infection control guidelines.

Avoid/pause chest compression during intubation

Remove PPE safely to avoid self-contamination and perform thorough hand-hygiene with soap and water

APPENDIX 4. “Dry nebulization” protocol metered-dose inhaler (MDI) with spacer/valved-holding chamber (VHC) (Adapted from the protocol of National University Hospital, Singapore)

“Dry nebulization” protocol using metered-dose inhaler (MDI) with spacer/ valved-holding chamber (VHC)
<ul style="list-style-type: none"> - Jet nebulization is associated with aerosol generation and can facilitate the transmission of viruses e.g. SARS and possibly 2019-nCoV. - To reduce the risk of disease transmission, we recommend the use of “dry nebulization” in the treatment of acute airflow obstruction. - This is clinically equivalent to nebulization therapy in patients with moderate to severe airflow obstruction.
Instructions
<p>1. Selection of spacer or VHC Choose one with a mouthpiece of facemask depending on your patient’s ability to maintain effective seal (e.g. children, elderly with cognition, acute breathless patients) Prime the new spacer by firing ~ 10 puffs of Salbutamol to reduce the static build-up inside (check product information sheet).</p>
<p>2. Preparation Remove the cap of MDI Shake the inhaler 5-10 times Insert into back of spacer or VHC.</p>
<p>3. Ensure an effective seal Face mask: Place mask over the mouth and nose and ensure minimal gaps Mouthpiece: Put mouthpiece in mouth between teeth and close lips around it.</p>
<p>4. Slow breathing Instruct the patient to breathe in and out <u>slowly</u>. Tell patient to slow down breathing if the spacer/VHC whistles.</p>
<p>5. Administer 1 puff at a time (to reduce clumping of particles) Press the canister <u>once</u> at the beginning of a slow inhalation. Instruct patient to take in 5 slow breaths (“Breathe in and out slowly, 5 times”)</p>
<p>6. Breath-hold for 5 to 10 seconds (<i>optional</i>) Instruct patient to hold breath for 5 to 10 seconds, if he/ she is able to cooperate. This allows the medication time to deposit in the airways. Resume normal breathing</p>

<p>7. Repeat steps 2-6 when more than 1 puff is prescribed.</p> <p>Initial treatment: repeat order every 10-20 min for 1st hour Subsequent treatment: Reduce frequency to every 4-8 hourly-prn Reduce/ stop ipratropium after initial 24 hours*</p>	
<p>8. Escalate in event of poor response:</p>	
<p>Severe features⁴</p> <ol style="list-style-type: none"> 1. Talks in words only, agitated <ul style="list-style-type: none"> - Respiratory rate > 30/ min - Pulse rate > 120/min - SpO2 < 90% (room air) 	<p>Life-threatening</p> <ul style="list-style-type: none"> - Drowsy, confused - Silent chest on auscultation
<p>Medication prescription for “dry nebulization”</p>	
Salbutamol (100mcg)	4 puffs
Ipratropium (20mcg)*	4 puff (if available, if not available then use salbutamol only)
<p>Every 10-20 minute for 1st hour Every 4-8 hours-prn, subsequently</p>	
<p><i>*Ipratropium is administered in combination with short-acting beta-agonist (SABA), if there is poor response to initial SABA nebulization, during acute moderate to severe exacerbations. Though the 2007 NAEP guidelines suggest that Ipratropium can be dosed up to maximum of 8 puffs every 20 minutes for the first 3 hours in an emergency setting. This is an off-label recommendation. Both GINA 2019 and SIGN 2019 do not explicitly state the recommended dose in an acute setting. As the recommended maximal total daily dose of Ipratropium is 204mcg, we recommend stopping/ reducing the dose after the initial 1-3 hours.</i></p>	
<p>For patients with preexisting airway disease like asthma/COPD, regular long acting inhalers can be continued using MDI with spacer.</p> <p>If patient is unable to use or has poor response to dry nebulization, switching to conventional nebulization may be needed. Airborne precaution must be applied and patient should preferably be in isolation room.</p> <p>Use mesh nebulizer rather than jet nebulizer for mechanically ventilated patients where available.</p> <p>Since disconnecting the ventilator circuit and nebulization generates aerosols, Healthcare workers must use airborne precaution and use appropriate PPE while caring for such patients with COVID19</p>	

APPENDIX 5: Critical care management including ventilator adjustment and Adapted from Brigham and Women's Hospital COVID-19 Critical Care Clinical Guidelines

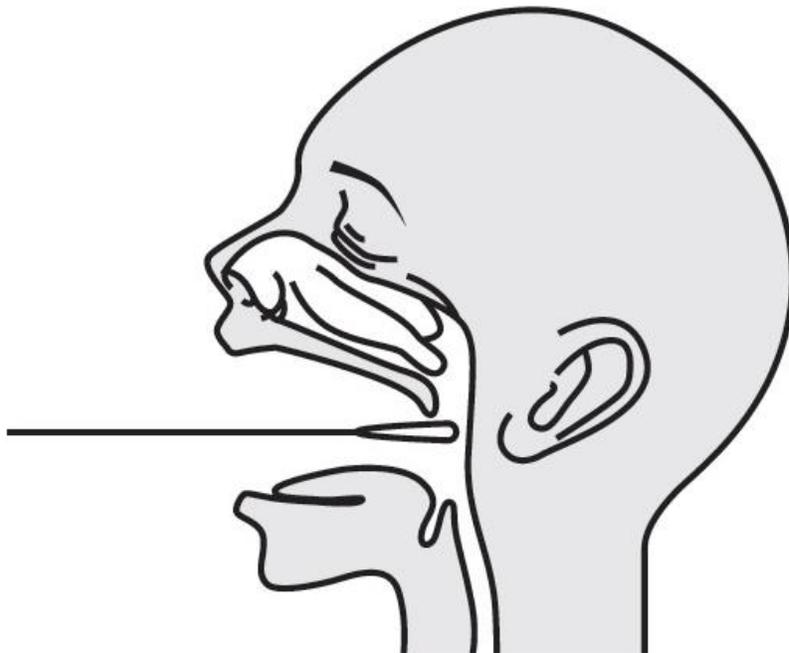
Ventilator adjustment and daily management
<p>Changing ventilation parameters</p> <ol style="list-style-type: none"> 1. Follow ARDSnet ventilation recommendations where possible: <ul style="list-style-type: none"> Tidal volumes should be 4-6 cc/kg using IBW to minimize volumes (and thus ventilator-associated injury). 2. Minute ventilation (respiratory rate x tidal volume) typically drives pH and PCO₂: <ul style="list-style-type: none"> Titrate ventilator parameters to pH, not PCO₂. - To achieve low tidal volumes, tolerate hypercapnia (functionally no limitation unless clinical sequelae) and acidemia (pH > 7.2). - Because tidal volumes are low, the respiratory rate often has to be high to accommodate; typical RR is 20-35 breaths/minute. 3. pH goal is normally 7.25-7.45: <ul style="list-style-type: none"> - If pH > 7.45, decrease respiratory rate - If pH 7.15-7.30, then increase respiratory rate until pH > 7.30, or PaCO₂ < 25 (maximum RR= 35 breaths/minute) • If pH < 7.15, then increase respiratory rate to 35 breaths/minute. If pH still < 7.15, then perform the following: <ol style="list-style-type: none"> a. Tidal volume may be increased by 1 mL/kg until pH > 7.15 (until plateau pressure reaches 30 cm H₂O or tidal volume reaches 8 ml/kg) b. Deep sedation advancing to RASS -5 if needed c. If no improvement, initiate continuous paralysis d. If still no improvement, initiate prone ventilation (may improve V/Q matching and better ventilation)
<p>Changing oxygenation parameters</p> <ol style="list-style-type: none"> 1. Minimize oxygen toxicity: PEEP and FiO₂ drive oxygenation <ul style="list-style-type: none"> - The goal is to deliver a partial pressure of oxygen to perfuse tissues (PaO₂ > 75, SpO₂ >92%) while limiting lung injury from high distending pressures (Ppl < 30) and hyperoxia (FiO₂ < 75, SpO₂ < 96%) - Lower limit goals for PaO₂ / SpO₂ are widely debated; PaO₂ > 55 and SpO₂ >88% are also commonly used. 2. Optimize PEEP: <ul style="list-style-type: none"> - Initial PEEP should be set as explained in the PEEP table below. 3. Adjust FiO₂: <ul style="list-style-type: none"> - Adjust FiO₂ after optimizing PEEP. - Goal FiO₂ < 75%; if FiO₂ > 75%; patient requires ventilator optimization. - It is reasonable to put a desaturating patient temporarily on 100% FiO₂, but remember to wean oxygen as rapidly as possible 4. Check plateau pressure: <ul style="list-style-type: none"> - Check plateau pressure with every change in tidal volume, PEEP, or clinical deterioration (worsening oxygenation) but not as part of routine practice - If plateau pressure is > 30 cm H₂O, then decrease tidal volume by 1 ml/kg (minimum 4 mL/kg). - If plateau pressure is < 25 H₂O and tidal volume < 6 mL/kg, then increase tidal volume by 1 mL/kg until plateau pressure is > 25 cm H₂O or tidal volume = 6 mL/kg. - If plateau pressure is < 30 cm H₂O and patient is breath stacking or dyssynchronous, then increase tidal volume in mL/kg increments to 7 mL/kg or 8 mL/kg so long as plateau pressure is < 30 cm H₂O.

Refractory hypoxemia pathway														
<p>If patient is hypoxic (PaO₂ <55) on V_t = 6 ml/kg, ideal PEEP and FiO₂ >75%, perform the following in this order:</p> <ol style="list-style-type: none"> Optimize volume status by diuresis or RRT if possible. <p>If no improvement, then:</p> <ol style="list-style-type: none"> Deep sedation, advancing to RASS -5 if needed. <p>If no improvement, then:</p> <ol style="list-style-type: none"> Initiate continuous paralysis using available paralyzing agents, titrated to patient-ventilator synchrony). <p>If no improvement then:</p> <ol style="list-style-type: none"> Initiate prone ventilation (see below); high consideration for use early in severe ARDS (<36 hours from ARDS onset, start discussion of proning when P:F< 150, prone within 12 hours of FiO₂ > 75%) <p>If no improvement then:</p> <ol style="list-style-type: none"> Consider ECMO if available 														
Titrate FiO₂ and PEEP for oxygenation for BMI<35 as per the ARDSnet LOW PEEP table														
FiO ₂	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	5	5	8	8	10	10	10	12	14	14	14	16	18	18-24
Titrate FiO₂ and PEEP for oxygenation for BMI>35 as per the ARDSnet HIGH PEEP table														
FiO ₂	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5	0.5	0.5-0.8	0.8	0.9	1.0	1.0
PEEP	5	8	10	12	14	14	16	16	18	20	22	22	22	24

APPENDIX 6: Ventilator Bundle

<p>Head-of-bed elevation 30 - 45°</p> <p>Daily sedative interruption</p> <p>Daily spontaneous breathing trial</p> <p>Deep vein thrombosis prophylaxis</p> <p>Stress ulcer prophylaxis (in patients with high risk of gastrointestinal bleeding)</p> <p>Subglottic secretion drainage in patients likely to be ventilated for more than 48 hours</p>

APPENDIX 7: Nasopharyngeal and oropharyngeal swab specimen collection



Source for images: www.stanfordlab.com and another online source that could not be verified on the internet

IX. CONTRIBUTORS

This document was prepared by the Nepal Medical Council COVID-19 Treatment Guidance Committee.

- Dr Anup Subedee (Co-ordinator)
- Prof. Dr Subhash P Acharya (Member, and representative from Nepalese Society of Critical Care Medicine)
- Dr Prabhat Adhikari (Member)
- Dr Pravindra Adhikari (Member, and representative from Nepal Dental Association)
- Asst. Prof. Dr Badri Rijal (Member, and representative from Nepal Medical Association)
- Dr Sanjeet Krishna Shrestha (Member, and representative from Society of Internal Medicine of Nepal)
- Dr Sanjeeb Tiwari (Member, and representative from General Practitioners Association of Nepal)
- Prof. Dr Sangita Basnet (Invited Expert)
- Prof. Dr Janak Koirala (Invited Expert)
- Dr Rakshya Pandey (Invited Expert)
- Dr Raju Pangen (Invited Expert)
- Prof. Dr Bhagawan Koirala (President, Nepal Medical Council)