GOVERNMENT OF THE REPUBLIC OF THE UNION OF MYANMAR

MINISTRY OF HEALTH

DEPARTMENT OF MEDICAL SERVICES

Clinical Management Guidelines for COVID-19 Acute Respiratory Disease

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Content

Clinical Management Guidelines for Coronavirus Disease (COVID-19)

Version (10/2023) (4-6-2023)

I. Case definitions for COVID-19

Suspected case of SARS-CoV-2 infection (3 options)

A. A person who meets the clinical ***OR*** epidemiological criteria:

Clinical criteria

- Acute onset of fever AND cough (ILI); ***OR***
- Acute onset of ANY THREE OR MORE of the following signs or symptoms: fever, cough, general weakness/fatigue[1], headache, myalgia, sore throat, coryza, dyspnea, anorexia/nausea/diarrhoea[1]

OR

Epidemiological criteria[2]

- Contact of a probable or confirmed case or linked to a COVID-19 cluster**.**[3]

B. A patient with severe acute respiratory illness (SARI: acute respiratory infection with history of fever or measured fever of ≥ 38 C°; and cough; with onset within the last 10 days; and requires hospitalization)

C. A person with no clinical signs or symptoms ***OR*** meeting epidemiologic criteria with a positive SARS-CoV-2 Antigen-RDT[4]

Probable case of SARS-CoV-2 infection (2 options)

A. A patient who meets clinical criteria ***AND*** is a contact of a probable or confirmed case, or linked to a COVID-19 cluster[3]

B. Death, not otherwise explained, in an adult with respiratory distress preceding death ***AND*** who was a contact of a probable or confirmed case or linked to a COVID-19 cluster[3]

Confirmed case of SARS-CoV-2 infection (2 options)

A. A person with a positive Nucleic Acid Amplification Test (NAAT), regardless of clinical criteria ***OR*** epidemiological criteria

B. A person meeting clinical criteria ***AND/OR*** epidemiological criteria (suspect case A) with a positive SARS-CoV-2 Antigen-RDT[4]

1 Signs separated with slash (/) are to be counted as one sign.

2 In light of the heightened transmissibility of emerging variants and the high likelihood that any close contact could be infected, epidemiological criteria alone are included in order to qualify asymptomatic contacts for testing, when possible, for the countries with the capacity to adapt more sensitive testing strategies; this is particularly relevant in high-risk populations and settings

3 A group of symptomatic individuals linked by time, geographic location and common exposures, containing at least one NAAT-confirmed case or at least two epidemiologically linked, symptomatic (meeting clinical criteria of Suspect case definition A or B) persons with positive Ag RDTs (based on ≥97% specificity of test and desired >99.9% probability of at least one positive result being a true positive)

4 Ag RDT antigen-detection rapid diagnostic tests (Ag RDT) are available for use by trained professionals or for self-testing by individuals:

-Professional-use SARS-CoV-2 antigen-RDT: WHO EUL-approved Ag-RDT, in which sample collection, test performance and result interpretation are done by a trained operator

-Self-test SARS-CoV-2 antigen-RDT: WHO EUL-approved Ag-RDT in which sample collection, test performance and result interpretation are done by individuals by themselves.

Definition of a contact

A contact is a person who has had any one of the following exposures to a probable or confirmed case:

- face-to-face contact with a probable or confirmed case within 1 meter and for at least 15 minutes;
- direct physical contact with a probable or confirmed case;
- direct care for a patient with probable or confirmed COVID-19 disease without the use of recommended personal protective equipment; or
- other situations as determined by local health authorities based on local risk assessments.

Exposure must have occurred during the infectious period of the case, and defined as follows:

- Exposure to a symptomatic case: 2 days before and 10 days after symptom onset of the case, plus 3 days without symptoms or 3 days with improving symptoms, for a minimum period of 13 days after symptoms onset.
- Exposure to an asymptomatic case: 2 days before and 10 days after the date on which the sample that led to confirmation was taken.
- Contacts should be managed in the same way as for a symptomatic case.

NOTE:

- *All contacts who in the last 90 days have (i) completed the primary series vaccination, or (ii) have received a vaccine booster dose, or (iii) have reported a previous COVID-19 infection do not need to quarantine.*
- *Contacts at high risk and those living in high-risk settings, who have not completed a primary series or received a booster vaccine dose, or who have not reported a previous infection in the last 90 days, need to quarantine for 10 days. Quarantine can be shortened to 5 days if the contact tests negative on day 5 and presents no symptoms.*
- *Under uncertain situations (such as the emergence of a new variant of concern, or as otherwise indicated by assessments conducted by national health authorities), all contacts should quarantine for 14 days as a precautionary measure, although this period could be shortened with testing, if the characteristics of the new variant and detection methods for it are suitable.*

Management Protocol for Covid-19 Acute Respiratory Disease (*Version 10.1*)
(updated as of 1-6-2023)

Attendance of patients in hospital, OPD and community clinics

At triage area

A History of close contact with a confirmed or probable COVID-19 case

B
- Acute onset of fever *AND* cough (ILI); ***OR***
- Acute onset of *ANY THREE OR MORE* of the following signs or symptoms: fever, cough, general weakness/fatigue[1], headache, myalgia, sore throat, coryza, dyspnea, anorexia/nausea/diarrhoea

C Presenting fever and symptoms of severe acute respiratory disease with onset within the last 10 days

A
- Report to respective State and Regional or District or Township Health Department
- Follow CEU guidelines for clinical investigation form and laboratory guidelines for specimen collection

B / **C**
- Isolate the patient in a separate room (e.g., Fever room)
- Take strict IPC measures depending on severity
- Take complete and detail history and physical examination
- Inform Regional/Facility Level Clinical Management Committee

Person Under Investigation (PUI) for suspected pneumonia

- Move the patient to isolation room
- Take specimen and test at designated laboratories (To follow specimen collection guidelines)
- If clinician strongly suspect possibility of COVID-19 infection, second swab should be considered
- Follow "**Clinical Management Guidelines for Corona virus disease (COVID-19)**"
- Inform to DoMS, CEU, State/ Regional or District or Township Health Department

Mild pneumonia (PUI)
Symptomatic treatment

Pneumonia (Suspected)
Symptomatic treatment
Oral antibiotics

Severe Pneumonia (Suspected)
(If any of following signs/symptoms is present)
- Respiratory rate > 30 breaths/min
- Severe respiratory distress
- SpO_2 < 90% on room air
- Systolic Blood Pressure ≤ 100 mmHg
- Altered mental status (GCS <15)

Result (+)

Result (–)

Discharge

Discharge criteria

Discharge message

Recover

Result (+)

- High flow O_2 5L/min
- Supportive treatment including fluid therapy
- IV empiric antibiotics
- Treatment of complications
- Assess for ventilator & specialist care

Result (+)

Confirmed case
- Supportive treatment including fluid therapy
- Antibiotic if indicated
- Antiviral, immunomodulators and thromboprophylaxis (To follow algorithm)
- Monitor disease progression and complication
- Refer to designated hospital/center with standard precaution and considering risk and benefit
- Isolate the patient until he/she meets discharge criteria

Death – proper disposal of the dead person

II. History taking

Name: ---------- Age: ----------
Sex: ---------- R/N: ----------
Address: ----------
Detail of Travel History----------
Contact History----------

Complaints

Fever ……Cough …… Fatigue…… Anorexia ……Shortness of breath …..…Myalgia ……. Sore throat……. Nasal congestion……Headache……. Diarrhea…..... Nausea & Vomiting …… Loss of smell……Loss of taste……Conjunctivitis (especially in children) ……...
Others ……dizziness……agitation……. weakness……. seizures……. trouble with speech or vision……. sensory loss……. problems with balance in standing or walking……
(Older people and immunosuppressed patients in particular may present with atypical symptoms such as fatigue, reduced alertness, reduced mobility, diarrhea, loss of appetite, confusion, and absence of fever)

III. Physical examination

Vital signs: GCS: …… Temperature……. Cyanosis……. BP: ….. ……
HR: …… SpO2: …… RR: …….. Lungs: ……..
Features of Septic shock, ARDS, Acute kidney injury etc.

IV. Risk factors for severe disease

- Age more than 60 years (increasing with age).
- Underlying noncommunicable diseases (NCDs): diabetes, hypertension, cardiac disease, chronic lung disease, cerebrovascular disease, dementia, mental disorders, chronic kidney disease, immunosuppression, obesity and cancer.
- In pregnant or recently pregnant: women > 35 years old, obesity, with chronic medical conditions or pregnancy specific disorders (e.g. gestational diabetes and pre-eclampsia/eclampsia).
- Smoking.
- Unvaccinated against COVID-19.
- HIV.

V. Disease severity classification for COVID-19

<u>Mild disease</u>

- Symptomatic patients meeting the case definition for COVID-19 without evidence of viral pneumonia or hypoxia.

<u>Moderate disease</u>

- Adolescent or adult with clinical signs of pneumonia (fever, cough, dyspnoea, fast breathing) but no signs of severe pneumonia, including $SpO_2 \geq 90\%$ on room air.
  Caution: The oxygen saturation threshold of 90% to define severe COVID-19 is arbitrary and should be interpreted cautiously. For example, clinicians must use their judgment to determine whether a low oxygen saturation is a sign of severity or is normal for a given patient with chronic lung disease.

Severe disease

- Adolescent or adult with clinical signs of pneumonia (fever, cough, dyspnoea) plus one of the following: respiratory rate > 30 breaths/min, severe respiratory distress, or SpO_2 < 90% on room air.

Critical disease

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

Adult respiratory distress syndrome (ARDS)

- Onset: within 1 week of a known clinical insult (i.e. pneumonia) or new or worsening respiratory symptoms.
- Chest imaging: (radiograph, CT scan, or lung ultrasound): bilateral opacities, not fully explained by volume overload, lobar or lung collapse, or nodules.
- 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.

Oxygenation impairment in adults:

- Mild ARDS: 200 mmHg < PaO2/FiO2 ≤ 300 mmHg (with PEEP or CPAP ≥ 5cmH2O).
- Moderate ARDS: 100 mmHg < PaO2/FiO2 ≤ 200 mmHg (with PEEP ≥ 5 cmH2O).
- Severe ARDS: PaO2/FiO2 ≤ 100 mmHg (with PEEP ≥ 5 cmH2O).

Sepsis

- Acute life-threatening organ dysfunction caused by a dysregulated host response to suspected or proven infection. Signs of organ dysfunction include: altered mental status(delirium), difficult or fast breathing, low oxygen saturation, reduced urine output, fast heart rate, weak pulse, cold extremities or low blood pressure, skin mottling, laboratory evidence of coagulopathy, thrombocytopenia, acidosis, high lactate, or hyperbilirubinemia.

Septic shock

- Persistent hypotension despite volume resuscitation, requiring vasopressors to maintain MAP ≥ 65 mmHg and serum lactate level > 2 mmol/L.

VI. Investigations

Test for diagnosis of COVID-19

- NAAT testing (eg. Gene Xpert, RT-PCR)
  - ✓ Recommend for the diagnosis of COVID-19.
- Antigen detection (Ag-RDTs)
  - ✓ Typically, less sensitive than NAAT.
  - ✓ Should be prioritized for use in symptomatic individuals in the first 5-7 days since onset of symptoms and to test asymptomatic individuals at high risk of infection, including contacts and health workers, particularly in settings where NAAT testing capacity is limited.
  - ✓ In cases where NAAT is unavailable or where prolonged turnaround times preclude clinical utility, antigen testing can also be done.
- Specimen collection (Use appropriate PPE)
  - ✓ Upper respiratory tract – nasopharyngeal or oropharyngeal specimens in the first week of symptom onset
  - ✓ Lower respiratory tract - expectorated sputum, or endotracheal aspirate/bronchoalveolar lavage in ventilated patient if readily available

- SARS-CoV-2 antibody tests are not recommended for diagnosis of current infection with COVID-19.

Additional tests

- Depending on the local epidemiology and clinical symptoms, test for other potential etiologies (e.g. influenza, malaria, dengue fever, typhoid fever) as appropriate.
- For COVID-19 patients with severe or critical disease, also collect blood cultures (if, ideally prior to initiation of antimicrobial therapy).
- CP, CRP/ESR, RBS, U&E, Creatinine, ECG, CXR (PA), and if possible LFT with enzymes, D-dimer and ABG

Recommendations for laboratory testing

- Any suspected case should be tested for COVID-19 infection using available molecular tests or rapid antigen test.
- Based on clinical judgment, clinicians may opt to order a test for COVID-19 in a patient not strictly meeting the case definition, for example, if there are patients involved in a cluster of acute respiratory illness among healthcare workers or of severe acute respiratory infection (SARI) or pneumonia in families, workplaces or social network.
- If clinicians strongly suspect possibility of covid-19 infection, 2nd swab should be considered in PUI cases (if 1st swab test is negative).

VII. Immediate implementation of IPC measures (Should start at the point of entry to hospitals)

At triage

- Screening should be done at first point of contact at the emergency department or outpatient department.
- Give suspect patient a medical mask and direct patient to 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 standard precaution

- Hand hygiene (alcohol based hand rub/water and soap), use of PPE to avoid indirect and direct contact with patients' blood, body fluids, 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.

Apply droplet precaution

- Use medical mask if working within 1-2 meters of the patient.
- Use eye protection (face-mask or goggles)
- Place patients in single rooms, or group together those with the same etiological diagnosis.
- Limit patient movement within the institution and ensure that patients wear medical masks when outside their rooms.

Apply contact precaution

- Use PPE (medical mask, eye protection, gloves and gown) when entering room and remove PPE when leaving.
- If possible, use either disposable or dedicated equipment (e.g. stethoscopes, blood pressure cuffs and thermometers).
- If equipment needs to be shared among patients, clean and disinfect between each patient use.

- Minimal movement of patients or transport as much as possible.

Apply air-borne precaution

- Use PPE, including gloves, long-sleeved gowns, eye protection, and fit-tested particulate respirators (N95 or equivalent, or higher level of protection) when healthcare workers performing aerosol-generating procedures (i.e. open suctioning of respiratory tract, intubation, bronchoscopy, cardiopulmonary resuscitation).
- Avoid the presence of unnecessary individuals in the room.
- Care for the patient in the same type of room after mechanical ventilation commences.

VIII. Treatment

Treatment of mild COVID-19

- Isolate the patients in designated areas to contain virus transmission
- Symptomatic treatment such as antipyretics (paracetamol) for fever and pain
- Adequate nutrition and hydration
- Counsel about signs and symptoms of complications that should prompt urgent care such as difficulty in breathing, chest pain, etc.
- Educate about monitoring of vital signs and use of pulse oximeter.
- Antibiotic therapy/prophylaxis is not recommended

Treatment of moderate COVID-19: Pneumonia treatment

- Isolate the patients in designated areas to contain virus transmission
- Antibiotics if there is clinical suspicion of bacterial infection
- Monitor the patients for signs and symptoms of disease progression (eg. respiratory distress, reduced SpO2 <90%, hypotension, etc.)

Treatment of severe COVID-19: Severe Pneumonia treatment

- Immediate administration of supplemental oxygen therapy to target SpO2 ≥ 94% and to any patient without emergency signs and hypoxaemia (i.e. stable hypoxaemic patient) to target SpO2 > 90% or ≥ 92–95% in pregnant women.
- Monitor for signs of clinical deterioration, such as rapidly progressive respiratory failure and shock
- Cautious fluid management in patients with COVID-19
- Use of empiric antimicrobials to treat all likely pathogens, based on clinical judgment, patient host factors and local epidemiology, within 1 hour of initial assessment if possible, ideally with blood cultures obtained first. Antimicrobial therapy should be assessed daily for de-escalation.
- Adults with emergency signs (obstructed or absent breathing, severe respiratory distress, central cyanosis, shock, coma and/or convulsions) should receive emergency airway management and oxygen therapy.

For patients with ARDS	-	Refer to ICU management *(See details in Annex)*
For patients with septic shock	-	Early diagnosis and supportive treatment within 1 hour of recognition
	-	IV fluid resuscitation (250-500 ml crystalloid fluid as rapid bolus in first 15-30 minutes
	-	Do not use hypotonic crystalloids, starches or gelatins for resuscitation

- Administer vasopressors (Noradrenalin) when shock persists during or after fluid resuscitation to reach MAP 65 mmHg
- Consider dobutamine if sings of poor perfusion and cardiac dysfunction persists despite achieving MAP target with fluids and vasopressors

Prevention of complications in hospitalized and critically ill patients with COVID-19

- Monitor patients with COVID-19, for signs or symptoms suggestive of thromboembolism, such as stroke, deep venous thrombosis, pulmonary embolism or acute coronary syndrome.
- *In hospitalized patients with COVID-19,* suggestion for administering thromboprophylaxis are according to "Algorithm for Therapeutic Management of hospitalized adult patients with COVID-19 April 2023"
- Suggested dosing of standard thromboprophylaxis is as follows:
    - Enoxaparin 40 mg by subcutaneous injection every 24h:
    - *Prophylactic dosages (non-weight adjusted) in low body weight (women < 45 kg, men < 57 kg) may lead to a higher risk of bleeding.*
    - Unfractionated heparin (UFH) 5000 units by subcutaneous injection every 8 or 12h:
    - *If BMI > 40 kg/m2 or weight > 120 kg: enoxaparin 40 mg by subcutaneous injection every 12h*
    - Fondaparinux 2.5 mg by subcutaneous injection every 24h.
    - duration of standard thromboprophylaxis is until hospital discharge.
    - Careful clinical observation is advised.
- Turn patient every two hours
- Awake proning position may reduce ICU admission (see attached photo)
- Give early enteral nutrition (within 24–48 hours of admission)
- Administer PPI in patients with risk factors for GI bleeding.
- Actively mobilize the patient early in the course of illness when safe to do so

Antivirals, immunomodulators and thromboprophylactic therapies for COVID-19 Disease

- Refer to Algorithm for Therapeutic Management of hospitalized adult patients with COVID-19 May 2023 and Algorithm for Antiviral treatment of adult patient with Covid-19 Omicron and related variants May 2023 *(See Algorithm in Annex)*

Treatment of neurological and mental manifestations associated with COVID-19

- Implement measures to prevent delirium
- Evaluate using standardized protocol for the development of delirium
- If detected, then immediate evaluation by a clinician is recommended to address any underlying cause of delirium and treat appropriately.
- Provide basic mental health and psychological support for all patients
- Prompt identification and assessment of anxiety and depressive symptoms
- Management of sleep problem in the context of acute stress

Patients presenting with rapidly developing neurological symptoms suggestive of stroke

- should be evaluated as soon as possible.

- standard stroke protocols should be followed including systemic thrombolysis and/or intra-arterial thrombectomy, if indicated.
- signs and symptoms of stroke can include weakness of limbs or face, sensory loss, speech difficulties, impairment of vision, ataxia, confusion, or decreased consciousness.
- standard IPC measures must be followed during the clinical evaluation, neuroimaging or procedures for patients with stroke.
- strokes can be missed in severely sick or unresponsive ICU patients and a low threshold for further evaluation (including neuroimaging) is recommended for acute neurological worsening.
  (See Acute stroke management pathway during COVID-19 pandemic in Annex)

Treatment of Non communicable disease and COVID-19

- Continue or modify previous medical therapy according to the patient's clinical condition to prevent drug interactions and adverse events
- Antihypertensive drugs should not routinely be stopped in patients with COVID-19
- Therapy may need to be adjusted based on general considerations for patients with acute illness, with particular reference to maintaining normal blood pressure and renal function.
- Attending physician should adjust therapy to maintaining normal blood pressure and renal function

IX. Rehabilitation for patients with COVID-19

- In hospitalized patients, during the acute phase of illness, interventions that relieve respiratory distress, prevent complications and support communication should be provided
- Prior to hospital discharge, COVID-19 patients should be screened for rehabilitation needs in order to facilitate onward referral.
- Education and support for the self-management of breathlessness and resumption of activities should also be provided.
- Arrange individualized rehabilitation programmes from subacute to long term according to patient needs.
- For those who experience persistent symptoms and/or limitations in functioning, screen for physical, cognitive and mental impairments, and manage accordingly.

Awake proning guide

Aims

Awake proning **may reduce** ICU admissions. Intubation in COVID19 has a high mortality. Patient **must** be **awake** and willing to **comply**.

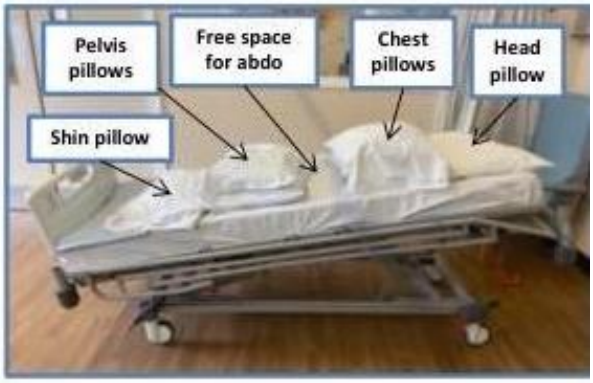
Duration

Aim to remain prone for **4 hours periods**. Allow **1 hour comfort breaks** between periods of proning for eating, drinking, toilet and general comfort.

Placement for patient positioning

-**1** soft pillow for the **head**
-**2** substantial pillows for under the **chest**
-**2** substantial pillows for under the **pelvis**
-**1** pillow for under the **shins**

NB: The abdomen should hang free and not be compressed. This is even more important in obese patients.



Bed position

Steep head up (at least **30 degrees**).

Head position

Leave oxygen mask in place – do not try and wean down immediately. Improvement of oxygenation with proning may take many hours to manifest.
Head turned to left or right – **whatever is comfortable** for the patient.

X. Discharge Criteria

(1) Discharge criteria for patients with SARS-CoV-2 infection *(See flow chart in Annex V)*

(2) Discharge criteria of contact patients from quarantine

- Hospital quarantine cases and contact of the COVID-19 confirmed cases should follow the updated quarantine guidelines of the Ministry of Health.

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Summary of revised facts

- Case definitions, History taking, Physical examination, Risk factors for severe disease, Disease severity classification, Antivirals, Immunomodulators, thromboprophylactic therapies, rehabilitation and discharge criteria have been updated
- Acute stroke management pathway during COVID-19 pandemic was added

Update plan

- Guidelines will be updated upon the new information and situation of the disease.

Contact

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Annex I

Standard Operating Procedure for use of Remdesivir in Patients with Confirmed COVID-19

- Remdesivir is a nucleoside drug. Its mechanism of action involves chain termination, which is different to lethal mutagenesis: the drug is incorporated preferentially to the endogenous adenosine nucleoside by the SARS-CoV-2 polymerase during replication of the RNA genome.
- In non-hospitalized patients with COVID-19, it reduces the risk of hospitalization.
- In hospitalized patients with severe COVID-19 who are not on mechanical ventilation, some data suggest it may reduce time to recovery and risk of mechanical ventilation.Guidelines from the IDSA, the NIH, and the WHO recommend remdesivir for severe COVID-19

Eligible persons

Adult non-hospitalized patients with who should meet the following criteria:

- Those with symptom onset within 10 days *and*
- Those at high risk of hospitalization (older age, immunosuppression and/or chronic diseases and lack of complete vaccination)

Hospitalized adult patients with severe COVID-19 who should meet the following criteria:

- Those with symptom onset within 10 days *and*
- Those who require supplemental oxygen through either low flow/high flow device or NIV but not on mechanical ventilation or ECMO

Contraindications

- Hypersensitivity to remdesivir or any component of the formulation
- Patients with eGFR <30 mL/minute, unless the potential benefit outweighs the potential risk
- ALT >10 times the ULN
- ALT elevation AND signs or symptoms of liver inflammation

Adverse reactions

- Endocrine & metabolic: Increased serum glucose
- Renal: Decreased creatinine clearance, increased serum creatinine
- Dermatologic: Skin rash
- Gastrointestinal: Nausea
- Hematologic & oncologic: Decreased hemoglobin, lymphocytopenia, prolonged prothrombin time
- Hepatic: Increased serum alanine aminotransferase, increased serum aspartate aminotransferase,
- Hypersensitivity: Hypersensitivity reaction
- Nervous system: Seizure
- Cardiovascular: Bradycardia, heart failure, hypotension

Drug Interactions

- Chloroquine: May diminish the therapeutic effect of Remdesivir. *Risk X: Avoid combination*
- CYP3A4 Inducers (Strong): May decrease the serum concentration of Remdesivir. *Risk C: Monitor therapy*

- Hydroxychloroquine: May diminish the therapeutic effect of Remdesivir. *Risk X: Avoid combination*

Dosing:

For non-severe COVID-19

Intravenous injection: 200 mg as a single dose on day 1, followed by 100 mg once daily on days 2 and 3.

Administration: IV infusion over 30 to 120 minutes. Flush line with at least 30 mL of NS after remdesivir infusion is complete

Duration: Total 3 days

For severe COVID-19

Intravenous injection: 200 mg as a single dose on day 1, followed by 100 mg once daily on day 2 to day 5.

Administration: IV infusion over 30 to 120 minutes. Flush line with at least 30 mL of NS after remdesivir infusion is complete

Duration: Total 5 days

Dosing: Renal Impairment

- eGFR ≥30 mL/minute: No dosage adjustment necessary
- eGFR <30 mL/minute: Use not recommended unless potential benefit outweighs potential risk

Dosing: Hepatic Impairment

Baseline hepatic impairment: There are no dosage adjustments provided in the manufacturers labeling.

Pregnancy considerations

- Generally, offer treatment with remdesivir when indicated and after a risk-benefit discussion with the patient.
- No data are available on placental transfer in humans. Data on pregnancy outcomes in patients with COVID-19 treated with remdesivir are limited and confounded by the severity of disease and disease complications in these patients

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Annex II

ICU MANAGEMENT GUIDELINE OF ACUTE HYPOXEMIC RESPIRATORY FAILURE AND ARDS WHEN COVID-19 INFECTION IS SUSPECTED (Updated as of 1-6-2023)

ICU admission criteria for COVID 19 patients

1. Patient requiring Invasive Mechanical Ventilation.
2. Patient requiring more than 2 hours on Non-Invasive Ventilation (NIV) or High Flow Nasal Cannula (HFNC).
3. Respiratory Distress,
   - Need O_2 > 15 LPM to maintain SpO_2 > 90%
   - Rapid escalation of oxygen requirement.
   - Significant work of breathing i.e. Tachypnea (RR > 35/min)
4. Patient with hemodynamic instability despite initial conservative fluid resuscitation.
5. Patient requires vasopressor support. (Noradrenaline > 0.1µ/kg/min)
6. Patient with a decreased level of consciousness (GCS <10/15)
7. Acidosis (If ABG is available) - ABG with pH < 7.3 or PCO2 > 55 or above patient's baseline. Lactate > 2mmol/l.
8. Patient with unstable vital signs not yet on vasopressors.
9. Patent with new ECG findings, including ischemia, arrhythmias, heart block.

Closed observation and monitoring, optimization of oxygenation to maintain SpO_2 > 90%

Exclusion criteria for ICU admission

1. Patient's wishes
2. Unwitnessed cardiac arrest, recurrent cardiac arrest, cardiac arrest with no ROSC
3. Malignant disease with a life expectancy of less than 12 months
4. Severe irreversible neurological event
5. NYHA class IV heart failure
6. COPD (Cor pulmonale who needs home oxygen therapy)
7. Liver cirrhosis (Child-Pugh score >8 or) with refractory ascites or encephalopathy > stage 1
8. Severe circulatory failure, treatment resistant despite increased vasoactive dose (hypotension and/or persistent inadequate organ perfusion).

   If one of the exclusion criteria is fulfilled, the patient is not to be admitted to ICU.

Criteria for endotracheal intubation should be based on individual situation. The followings are red signs;

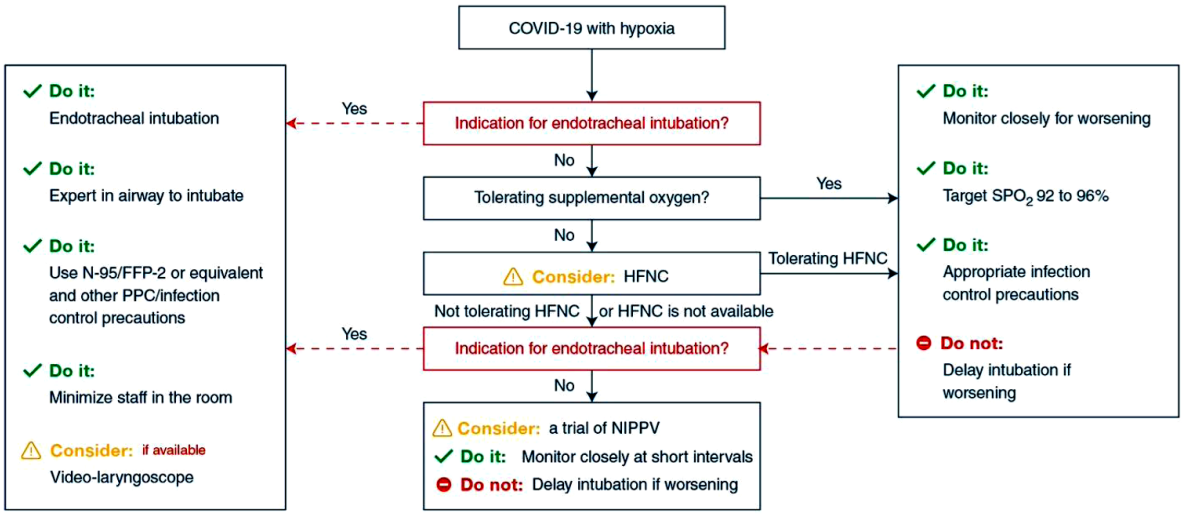
1. Respiratory rate > 35/min, severe respiratory distress with increased work of breathing
2. PaO_2/ FiO_2 < 200 (If ABG available) or SpO_2/FiO_2 <150
3. Severe acidosis pH <7.25 (If ABG available)
4. Altered mental status
5. Hemodynamic instability (MAP ≤ 65 mmHg) after fluid resuscitation and vasopressor/inotrope support) (according to updated SSC guideline Hour 1 bundle)

Ventilatory Support

- Conditional recommendation to use high-flow nasal oxygen (HFNO) in hospitalized patients with severe or critical COVID-19 and acute hypoxaemic respiratory failure (AHRF) not needing emergent intubation rather than standard oxygen therapy
- Conditional recommendation to use continuous positive airway pressure (CPAP) in hospitalized patients with severe or critical COVID-19 and acute hypoxaemic respiratory failure (AHRF) not needing emergent intubation rather than standard oxygen therapy
- Conditional recommendation to use non-invasive ventilation in hospitalized patients with severe or critical COVID-19 and acute hypoxaemic respiratory failure (AHRF) not needing emergent intubation rather than standard oxygen therapy

Close monitoring and short interval assessment for worsening of respiratory status and early intubation if worsening occurs is recommended.

For patients with persistent hypoxemia despite increasing supplemental oxygen requirements in whom endotracheal intubation is not otherwise indicated, consider a trial of awake prone positioning to improve oxygenation.



Endotracheal intubation must be followed the COVID-19 Airway management principles, WFSA guideline.

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. Rapid sequence intubation is appropriate after an airway assessment.

VENTILATOR SETUP AND ADJUSTMENT

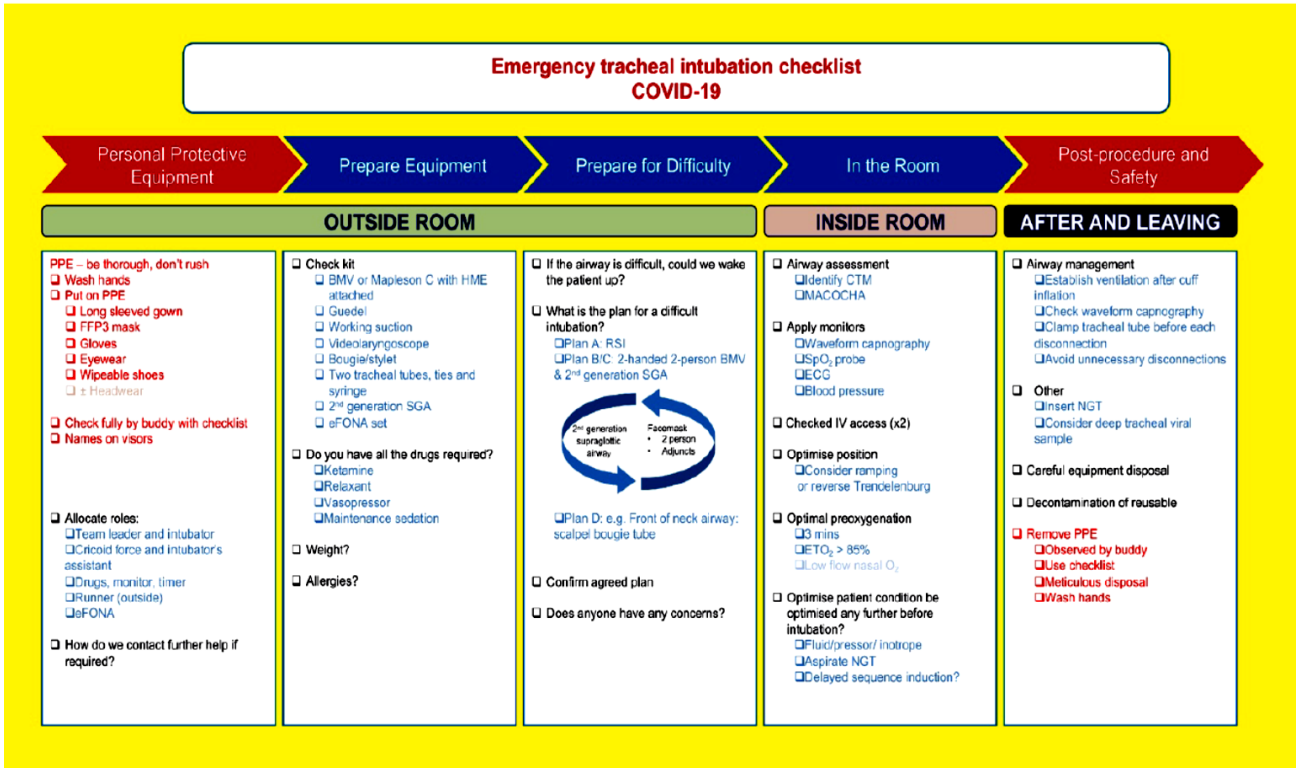
1. Calculate predicted body weight (PBW)
    a. Males = 50 + 2.3 [height (inches) - 60]
    b. Females = 45.5 + 2.3 [height (inches) -60]
2. Select any ventilator mode, AC or SIMV mode
3. Initial tidal volume is 6 ml/kg PBW; recommends using low tidal volume (VT) ventilation (VT 4–8 mL/kg of PBW) over higher tidal volumes (VT >8 mL/kg)
4. Set initial rate to approximate baseline minute ventilation (not > 35 bpm).
5. Adjust PEEP (5-15) and FiO2 to achieve SpO2 88-92% (PaO2- 55-80 mmHg) lower inspiratory pressures (plateau pressure <30 cmH2O).
6. The use of deep sedation may be required to control respiratory drive and to reduce the patient-ventilator dys-synchrony.
7. Use a conservative fluid management strategy for ARDS patients without tissue hypoperfusion.
8. In patients with moderate-severe ARDS (PaO2/FiO2 <150), neuromuscular blockade by continuous infusion should not be routinely used.
9. For mechanically ventilated adults and refractory hypoxemia despite optimized ventilation, recommend prone ventilation for 12 to 16 hours per day over no prone ventilation

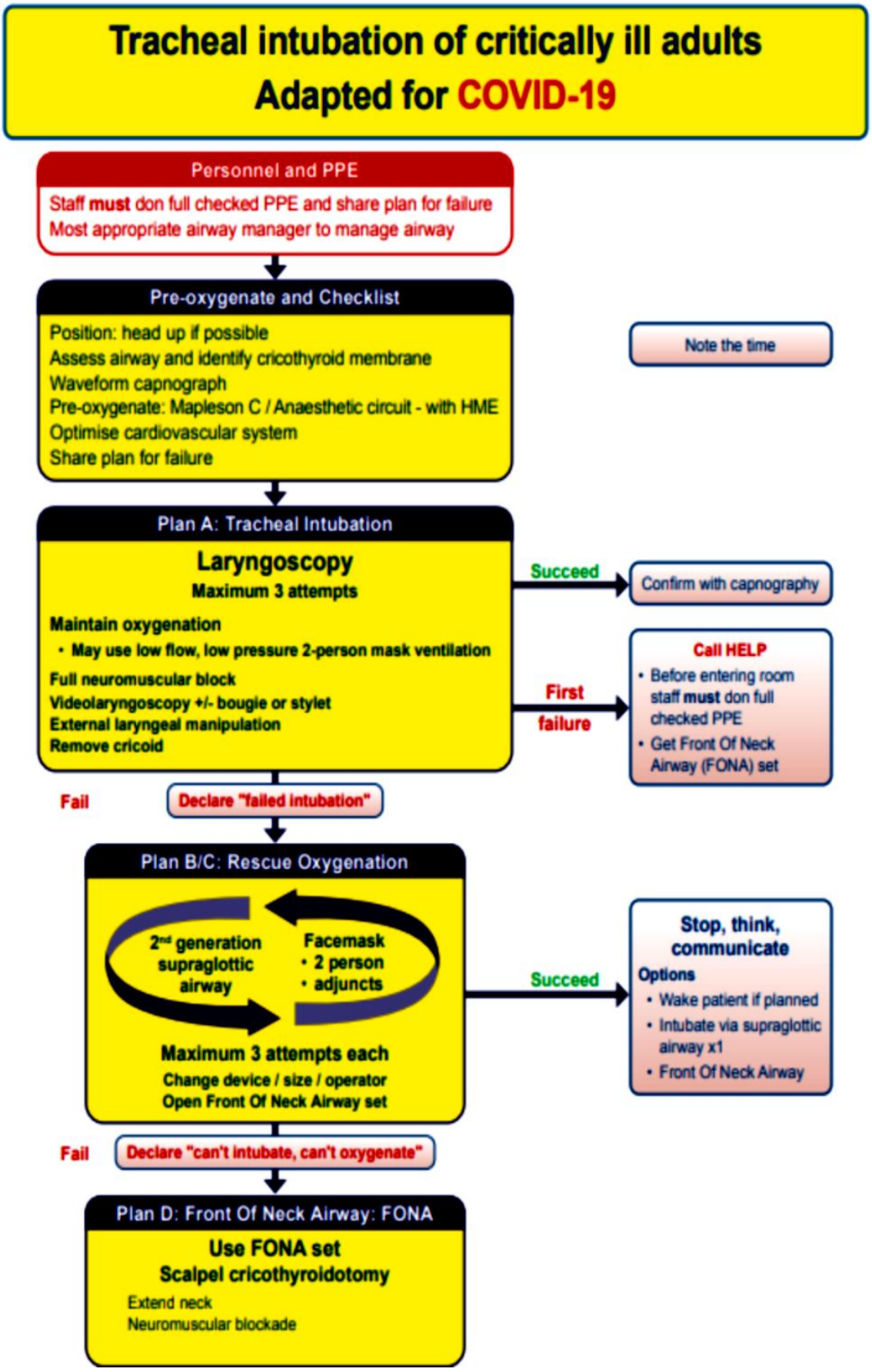
COVID-19 Airway management principles

High Risk Procedures – Tracheal Intubation and other Aerosol-generating medical procedures (e.g- endotracheal tube suction)

1. Limit staff present at tracheal intubation: one incubator, one assistant and one to administer drugs/monitor patient.
2. Preferably, the most experienced anaesthesiologist should perform the intubation.
3. Create a COVID-19 tracheal intubation trolley that can be used in ICU or elsewhere.
4. Aerosol-generating procedures (AGP) are in an adequately ventilated room and use appropriate PPE (N95 respirator, FFP2 or equivalent).
5. Everyone should know the plan before entering the room – use a checklist to achieve this.
6. Plan how to communicate before entering the room.
7. All preparations of airway equipment and drugs that can take place outside the room should do.

8. Before the procedure begins, ensure all equipment is ready: standard monitoring equipment, iv access, drugs. Ensure ventilator and suction equipment is functional.
9. Focus on safety, promptness and reliability. Aim to succeed at the first attempt because multiple attempts increase risk to sick patients and staff. Do not rush but make each attempt the best it can be.
10. Place an HME with viral filter between the catheter mount and the circuit at all times. Keep it dry to avoid blocking.
11. For tracheal suction, closed suction system should be used to prevent aerosol spread.
12. Use RSI with cricoid force where a trained assistant can apply it. Take it off if it causes difficulty. Five minutes of preoxygenation with oxygen 100% and RSI in order to avoid manual ventilation and potential aerosolization of infectious respiratory droplets. If manual ventilation is required, apply small tidal volumes only.
13. Endotracheal intubation perform using video-guided laryngoscopy, over direct laryngoscopy, if available.
14. To avoid cardiovascular collapse, use ketamine 1–2 $mg.kg^{-1}$, suxamethonium 1.5 $mg.kg^{-1}$.
15. Have a vasopressor for bolus or infusion (noradrenalin 0.05-1 µg/kg/min) immediately available for managing hypotension.
16. Communicate clearly: simple instructions, closed loop communication (repeat instructions back), adequate volume without shouting.
17. Place a nasogastric tube after tracheal intubation is completed and ventilation established safely.
18. Discard disposable equipment safely after use. Decontaminate reusable equipment fully and according to manufacturer’s instructions.


Emergency tracheal intubation checklist
COVID-19
Personal Protective Equipment
Prepare Equipment
Prepare for Difficulty
In the Room
Post-procedure and Safety
OUTSIDE ROOM
INSIDE ROOM
AFTER AND LEAVING
PPE – be thorough, don't rush
❑ Wash hands
❑ Put on PPE
❑ Long sleeved gown
❑ FFP3 mask
❑ Gloves
❑ Eyewear
❑ Wipeable shoes
❑ ± Headwear
❑ Check fully by buddy with checklist
❑ Names on visors
❑ Allocate roles:
❑Team leader and intubator
❑Cricoid force and intubator's assistant
❑Drugs, monitor, timer
❑Runner (outside)
❑aFONA
❑ How do we contact further help if required?
❑ Check kit
❑ BMV or Mapleson C with HME attached
❑ Guedel
❑ Working suction
❑ Videolaryngoscope
❑ Bougie/stylet
❑ Two tracheal tubes, ties and syringe
❑ 2nd generation SGA
❑ aFONA set
❑ Do you have all the drugs required?
❑Ketamine
❑Relaxant
❑Vasopressor
❑Maintenance sedation
❑ Weight?
❑ Allergies?
❑ If the airway is difficult, could we wake the patient up?
❑ What is the plan for a difficult intubation?
❑Plan A: RSI
❑Plan B/C: 2-handed 2-person BMV & 2nd generation SGA
2nd generation supraglottic airway
Facemask
• 2 person
• Adjuncts
❑Plan D: e.g. Front of neck airway: scalpel bougie tube
❑ Confirm agreed plan
❑ Does anyone have any concerns?
❑ Airway assessment
❑Identify CTM
❑MACOCHA
❑ Apply monitors
❑Waveform capnography
❑SpO2 probe
❑ECG
❑Blood pressure
❑ Checked IV access (x2)
❑ Optimise position
❑Consider ramping or reverse Trendelenburg
❑ Optimal preoxygenation
❑3 mins
❑ETO2 > 85%
❑Low flow nasal O2
❑ Optimise patient condition be optimised any further before intubation?
❑Fluid/pressor/ inotrope
❑Aspirate NGT
❑Delayed sequence induction?
❑ Airway management
❑Establish ventilation after cuff inflation
❑Check waveform capnography
❑Clamp tracheal tube before each disconnection
❑Avoid unnecessary disconnections
❑ Other
❑Insert NGT
❑Consider deep tracheal viral sample
❑ Careful equipment disposal
❑ Decontamination of reusable
❑ Remove PPE
❑Observed by buddy
❑Use checklist
❑Meticulous disposal
❑Wash hands


Tracheal intubation of critically ill adults
Adapted for COVID-19
Personnel and PPE
Staff must don full checked PPE and share plan for failure
Most appropriate airway manager to manage airway
Pre-oxygenate and Checklist
Position: head up if possible
Assess airway and identify cricothyroid membrane
Waveform capnograph
Pre-oxygenate: Mapleson C / Anaesthetic circuit - with HME
Optimise cardiovascular system
Share plan for failure
Note the time
Plan A: Tracheal Intubation
Laryngoscopy
Maximum 3 attempts
Maintain oxygenation
• May use low flow, low pressure 2-person mask ventilation
Full neuromuscular block
Videolaryngoscopy +/- bougie or stylet
External laryngeal manipulation
Remove cricoid
Succeed
Confirm with capnography
First failure
Call HELP
• Before entering room staff must don full checked PPE
• Get Front Of Neck Airway (FONA) set
Fail
Declare "failed intubation"
Plan B/C: Rescue Oxygenation
2nd generation supraglottic airway
Facemask
• 2 person
• adjuncts
Maximum 3 attempts each
Change device / size / operator
Open Front Of Neck Airway set
Succeed
Stop, think, communicate
Options
• Wake patient if planned
• Intubate via supraglottic airway x1
• Front Of Neck Airway
Fail
Declare "can't intubate, can't oxygenate"
Plan D: Front Of Neck Airway: FONA
Use FONA set
Scalpel cricothyroidotomy
Extend neck
Neuromuscular blockade

References;

(1) Clinical management of COVID-19: Living guideline, 23 June 2022 (WHO). https://www.who.int/publications-detail-redirect/WHO-2019-nCoV-clinical-2022-1

(2) Papazian L, Aubron C, Brochard L, et al. (2019) Formal guidelines: management of acute respiratory distress syndrome, *Annals of Intensive Care* , 9:69.

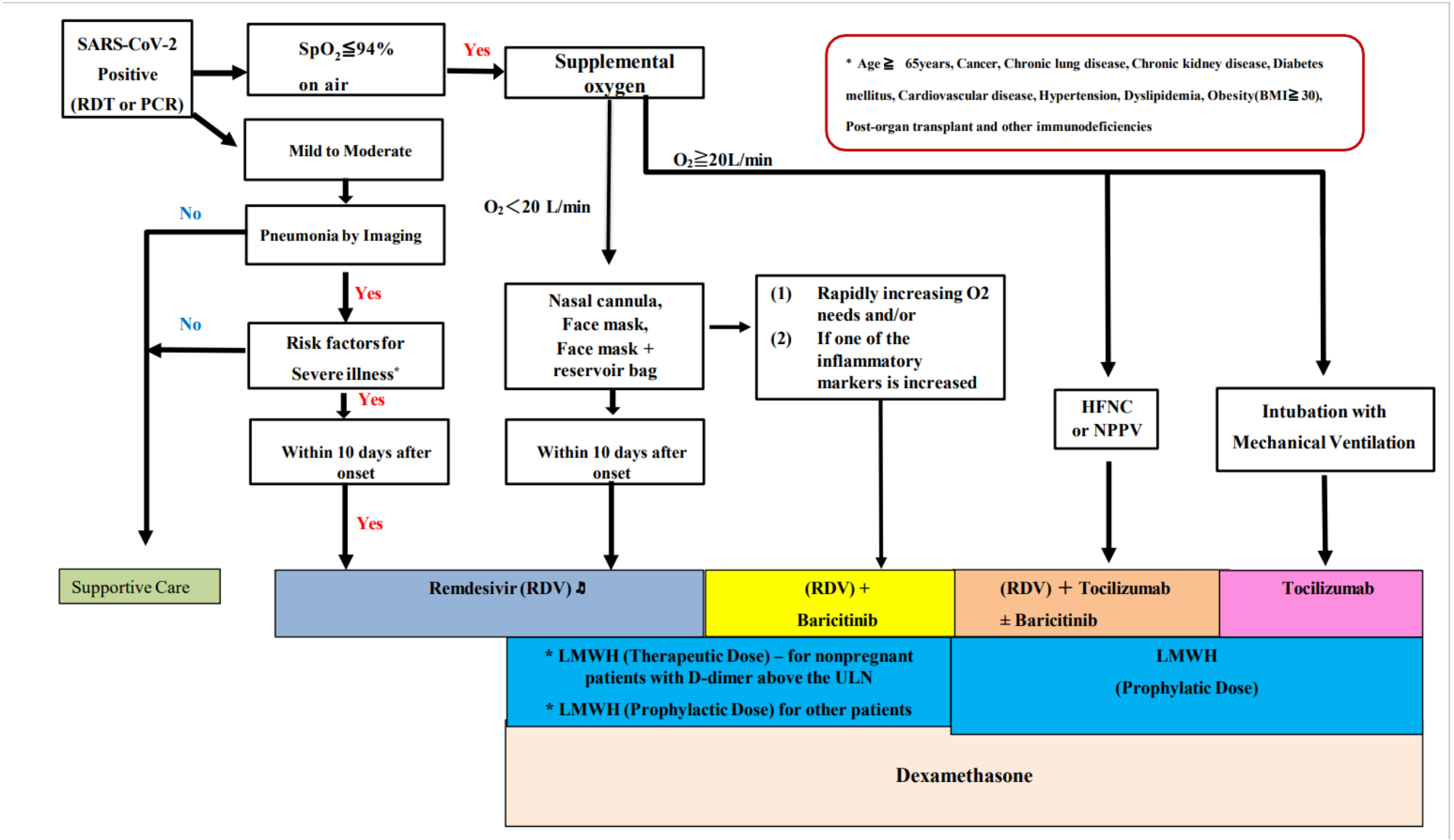
(3) COVID-19 Airway management principles (ICMANAESTHEAIACOVID-19.ORG)

(4) World Federation of Societies of Anaesthesiologists- Coronavirus- guidance for anaesthesia and perioperative care providers

(5) COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Available at https://www.covid19treatmentguidelines. nih.gov/.

Annex III

Algorithm for Therapeutic Management of hospitalized adult patients with COVID-19 (May 2023)



Drug name	**Dosage**	**Duration**	**Careful administration**	**Other information**
Remdesivir	**IV**: 200 mg as a single dose on day 1, followed by 100 mg once daily.	3 days, may extend up to 5 days	① eGFR< 30mL/min ② ALT >5 times the ULN	Up to 10 days in patients without substantial clinical improvement at day 5
Dexamethasone	**Oral, IV**: 6 mg as a single daily dose	7 to 10 days	① Active gastrointestinal bleeding ② hypersensitivity to dexamethasone	BW<40kg: 0.15mg/kg as a single daily dose
Tocilizumab	**IV**: 8mg/kg （maximum dose: 800mg） only once	1 day	① Possibly active tuberculosis ② ALT >5 times the ULN ③ Neutrophil count ＜ 500/mm^3 ④ Lymphocyte count ＜ 500/mm^3 ⑤ Platelet count ＜ 50,000/mm3	A screening test should be performed prior to administration; tuberculosis (chest X-ray and/ or IGRA), HBsAg, anti HCV Ab
Baricitinib	**Oral**: 4mg as a single dose 30≦eGFR＜60: 2mg as a single dose	Up to 14 days		

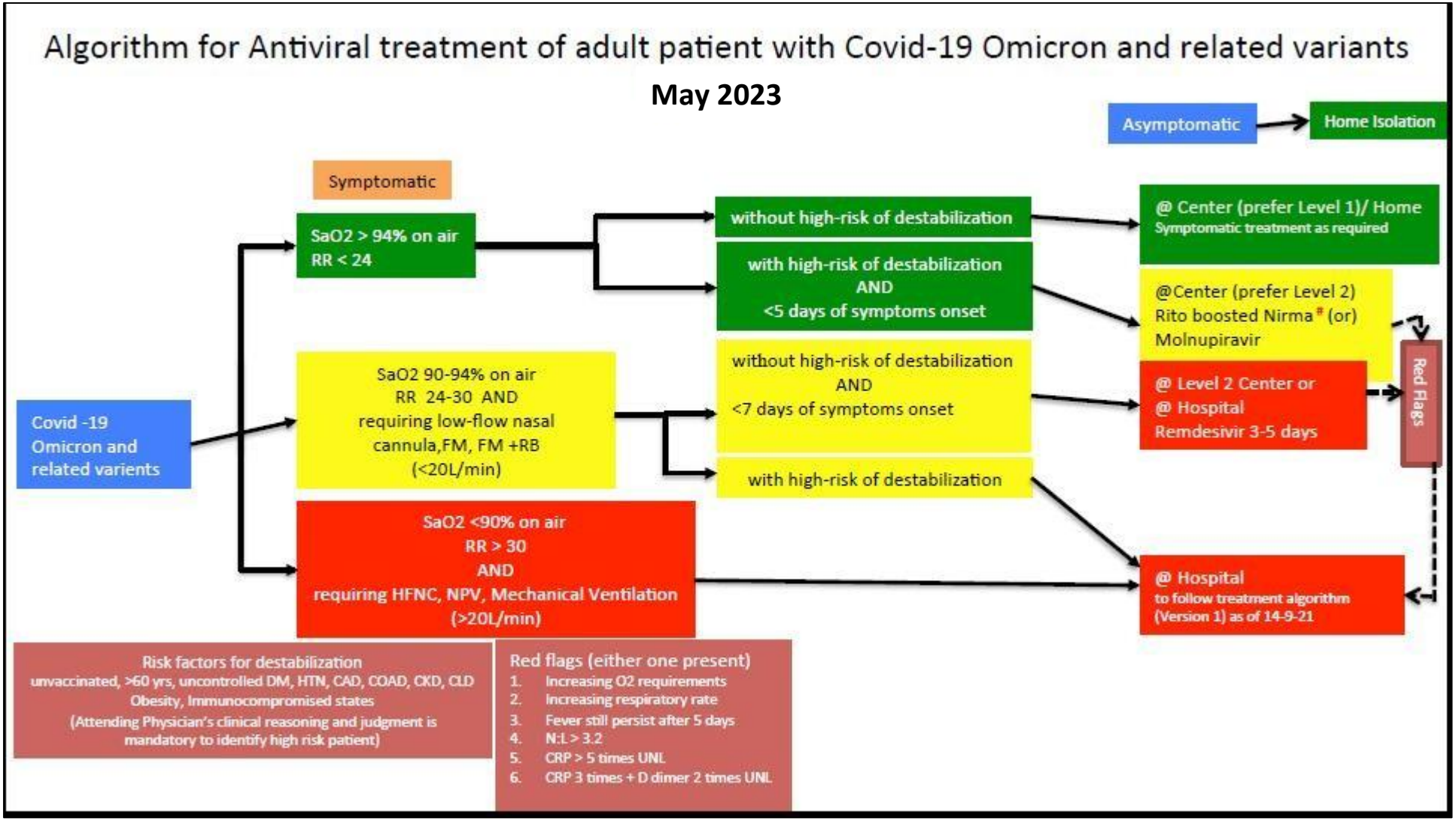
Remdesivir:

(1) Clinical reasoning and close supervision of attending Physician is necessary

(2) must be given in the hospital where laboratory facilities to monitor liver and renal function at least present

(3) risk and benefit should be weighed to use in patients with pregnancy and lactating mother

Annex IV


Algorithm for Antiviral treatment of adult patient with Covid-19 Omicron and related variants
May 2023
Asymptomatic
Home Isolation
Symptomatic
SaO2 > 94% on air
RR < 24
without high-risk of destabilization
with high-risk of destabilization
AND
<5 days of symptoms onset
@ Center (prefer Level 1)/ Home
Symptomatic treatment as required
@Center (prefer Level 2)
Rito boosted Nirma # (or)
Molnupiravir
Covid -19
Omicron and
related varients
SaO2 90-94% on air
RR 24-30 AND
requiring low-flow nasal
cannula,FM, FM +RB
(<20L/min)
without high-risk of destabilization
AND
<7 days of symptoms onset
@ Level 2 Center or
@ Hospital
Remdesivir 3-5 days
Red Flags
with high-risk of destabilization
SaO2 <90% on air
RR > 30
AND
requiring HFNC, NPV, Mechanical Ventilation
(>20L/min)
@ Hospital
to follow treatment algorithm
(Version 1) as of 14-9-21
Risk factors for destabilization
unvaccinated, >60 yrs, uncontrolled DM, HTN, CAD, COAD, CKD, CLD
Obesity, Immunocompromised states
(Attending Physician's clinical reasoning and judgment is
mandatory to identify high risk patient)
Red flags (either one present)
1. Increasing O2 requirements
2. Increasing respiratory rate
3. Fever still persist after 5 days
4. N:L > 3.2
5. CRP > 5 times UNL
6. CRP 3 times + D dimer 2 times UNL

Drug name	Dosage	Duration	Careful administration	Other information
Remdesivir	**IV**: 200 mg as a single dose on day 1, followed by 100 mg once daily.	3-5 days, may extend up to 10 days	① eGFR< 30mL/min ② ALT >5 times the ULN	Up to 10 days in patients without substantial clinical improvement at day 5
Molnupiravir	**Oral:** 800 mg BD	5 days	① may cause fetal harm if used in pregnancy ② contraindicated in those < 18 years of age	- Males with partners of childbearing potential: Advise to practice contraception up to 3 months after the last dose of Molnupiravir - Females of childbearing potential: Use a reliable method of contraception correctly during treatment and for 4 days after final dose
Ritonavir boosted Nirmatrelvir	Oral: Nirmatrelvir 300 mg + Ritonavir 100 mg bd	5 days	(1) eGFR> 30mL/min but < 60 ml/ min (2) Child-Pugh Class C (3) h/o TEN or Steven-Johnson Syndrome with these medications	- If the patient is taking atorvastatin or rosuvastatin, consider temporary discontinuation of atorvastatin and rosuvastatin during treatment - need additional contraceptive method if on OC pills - HIV antiretroviral medications can be co-administered without dose adjustment with the exception of Miraviroc

Indications for Ritonavir boosted Nirmatrelvir

Current diagnosis of mild to moderate COVID-19
- Age ≥ 18 years OR > 12 years of age and weighing at least 40 kg
- Has one or more risk factors for progression to severe COVID-19 (Healthcare providers should consider the benefit-risk for an individual patient.)
- Symptom onset within 5 days
- Not requiring hospitalization due to severe or critical COVID-19 at treatment initiation

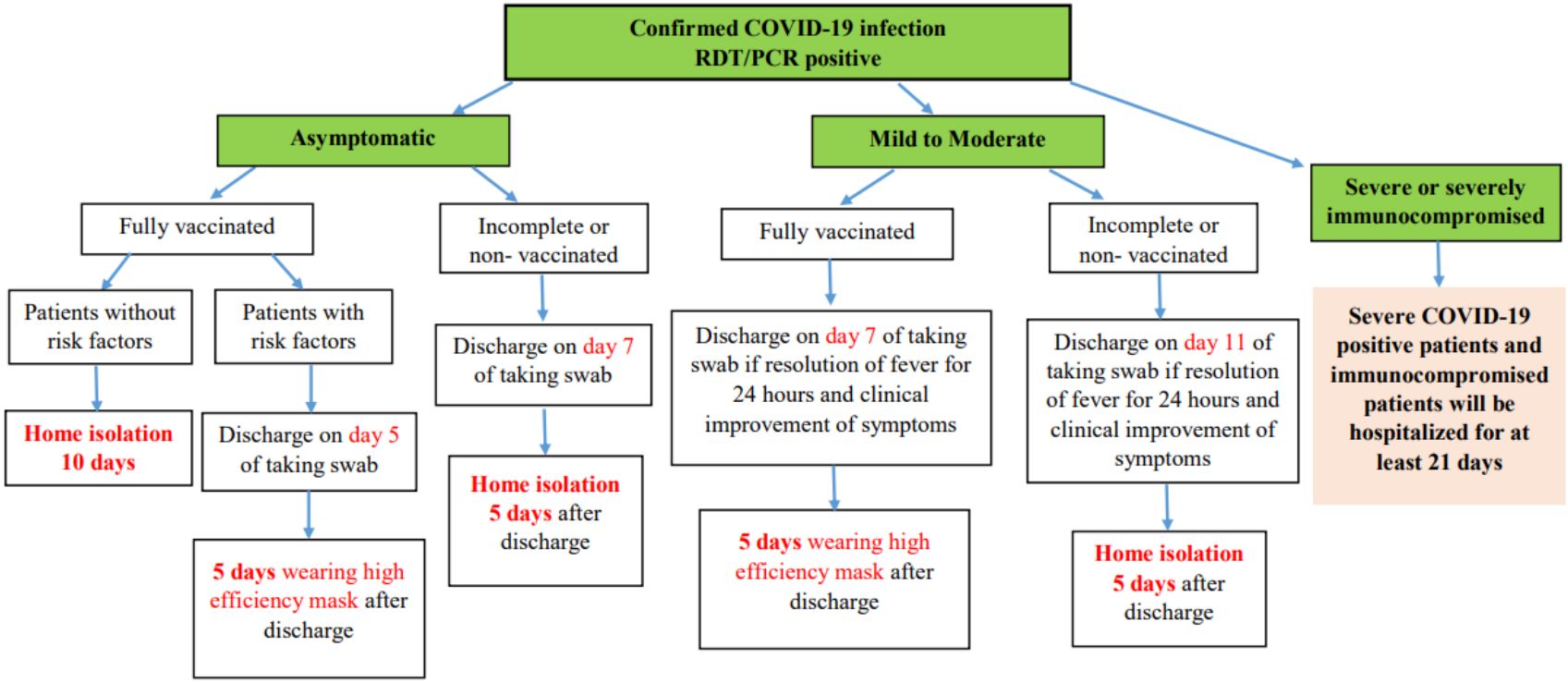
Annex V

THE GOVERNMENT OF THE REPUBLIC OF THE UNION OF MYANMAR

MINISTRY OF HEALTH

DEPARTMENT OF MEDICAL SERVICES

Discharge criteria of confirmed COVID-19 patients (Version 7) (as of 10-2-2022)

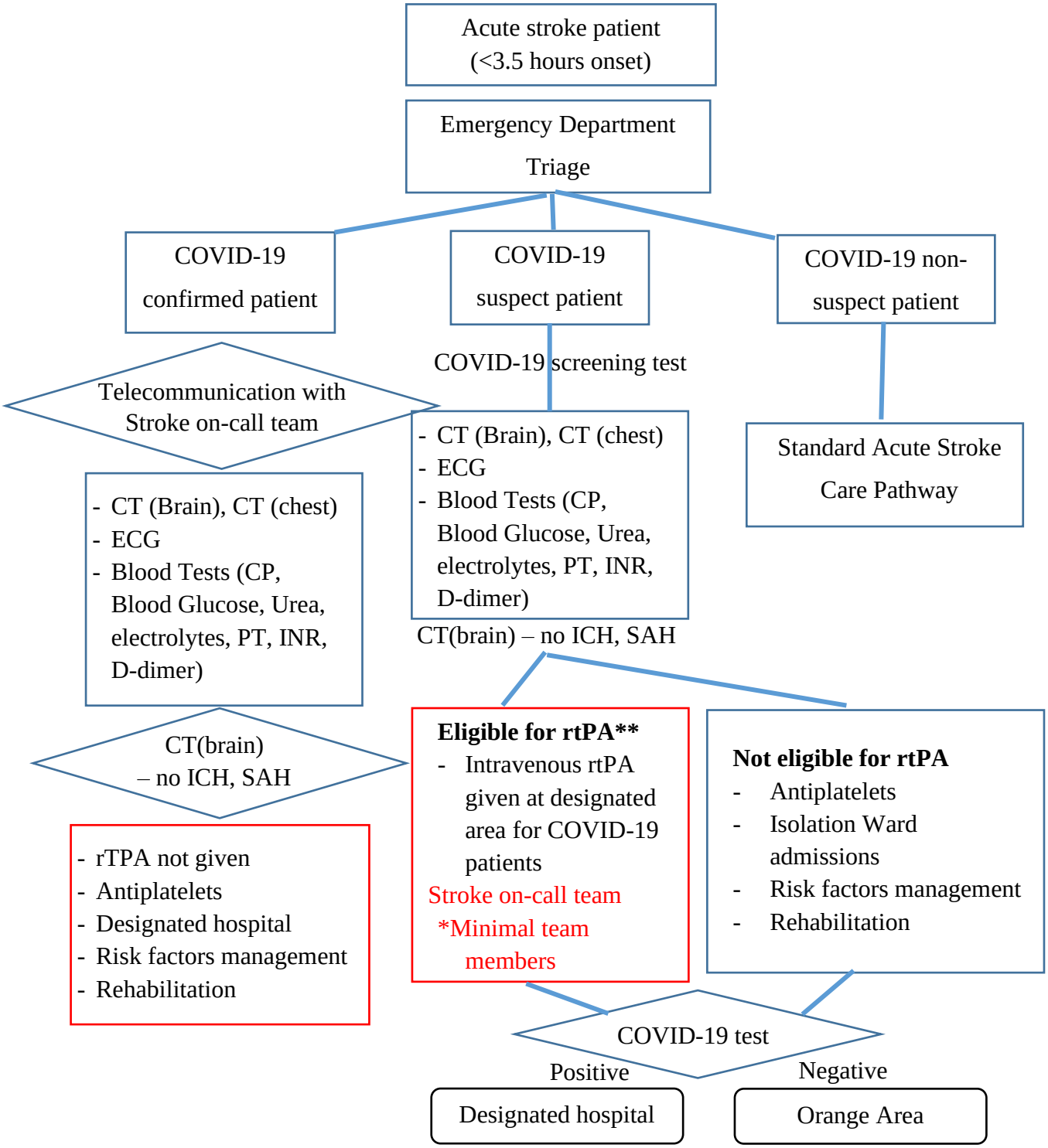


Risk factors – patients with comorbidities, elderly (>60 years), elderly at home, home without isolation facilities

DoMS COVID-19 DC criteria (version 7)(10-2-2022)

Annex VI

Acute stroke management pathway during COVID-19 pandemic



** Treatment decisions are individualized according to local guideline, precautions, protective measures and risk assessment

Anticoagulation treatment

- COVID-19 patients with high D dimer, non-AF ischemic stroke- can be given if no contraindications
- Anticoagulation treatment should not be used routinely for the treatment of acute stroke
- For most patients with a stroke or TIA in the setting of AF, it is reasonable to initiate oral anticoagulation within 14 days after the onset of neurological symptoms