Republic of Botswana

MINISTRY OF HEALTH & WELLNESS

Botswana COVID-19 Guideline 4:

Interim clinical guidance for the management of patients with Coronavirus disease 2019 (COVID-19) in Botswana

Version: 2.0 1st May 2020

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Foreword

On January 30, 2020, the International Health Regulations Emergency Committee of the World Health Organization (WHO) declared the Severe Acute Respiratory Syndrome due to novel coronavirus (SARS CoV-2) outbreak a "Public Health Emergency of International Concern" (PHEIC) and the WHO declared the outbreak a pandemic on 12th March 2020. Botswana stands ready to face the potential outbreak of SARS CoV-2.

Coronavirus disease 2019 (COVID-19) is pneumonia caused by a novel (new) Coronavirus with a high propensity to transmit from person-to-person. Asymptomatic carriage is possible, but transmission rates are not clear. Therefore, this calls for heightened vigilance. Whilst a cure or vaccine is still not yet available, optimized supportive care in a hospital setting has been shown to increase chances of survival among the critically ill, and preventative public health measures will mitigate the spread of infection in our communities.

Therefore, this document is an interim guide for use by health care workers taking care of adult patients suspected to have COVID-19 and for the management of confirmed cases. It is not meant to replace clinical judgement or specialist consultation, but rather to strengthen clinical management of these patients and provide up-to-date guidance which will be continuously updated as new evidence emerges.

We would like to acknowledge interim clinical guidance provided by our neighbours, South Africa[1] and Zambia[2], which has served as a template for our work.

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What has changed in this version?

Version 1.0, 2nd April 2020	First version
Version 2.0, 1st May 2020	Updated case definitions Screening algorithm updated (Figure 3) Clinical one-page summary added (Figure 4) VTE prophylaxis added (Figure 5) Discharge and deisolation criteria updated

Abbreviations and acronyms

ARDS	Acute Respiratory Distress Syndrome
ARI	Acute Respiratory Infection
ART	Antiretroviral Therapy
COVID-19	Coronavirus disease-19
FBC	Full Blood Count
Hb	Haemoglobin
HIV	Human Immunodeficiency Virus
ICU	Intensive Care Unit
IPC	Infection Prevention and Control
MERS CoV	Middle East Respiratory Syndrome Coronavirus
MoHW	Ministry of Health and Wellness
NHL	National Health Laboratory
PCR	Polymerase Chain Reaction
PEEP	Positive End-Expiratory Pressure
PLHIV	Persons living with HIV
PPE	Personal Protective Equipment
RT-PCR	Reverse Transcriptase Polymerase Chain Reaction
SARI	Severe Acute Respiratory Infection
SARS-CoV	Severe Acute Respiratory Syndrome Coronavirus
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronarvirus-2
TB	Tuberculosis
VTE	Venous thromboembolism
VTM	Viral Transport Medium
WHO	World Health Organization

1. Background

On 31st December 2019, the World Health Organization (WHO) was alerted to a cluster of pneumonia of unknown aetiology in patients in Wuhan City, Hubei Province of China. One week later the novel coronavirus (severe acute respiratory syndrome coronavirus 2: SARS-CoV-2) was identified as the cause[3]. The resulting illness was named COVID-19 on the 11th February 2020. The clinical spectrum of COVID-19 ranges from an asymptomatic or mild flu-like illness to a severe pneumonia requiring critical care[4]. These guidelines describe the approach to suspected cases of COVID-19, the clinical management of COVID-19 disease and covers clinical care in and outside health care facilities. It is intended for health care practitioners taking care of symptomatic patients with suspected or confirmed COVID-19. As the situation evolves these guidelines are likely to be updated.

2. Epidemiology and clinical characteristics

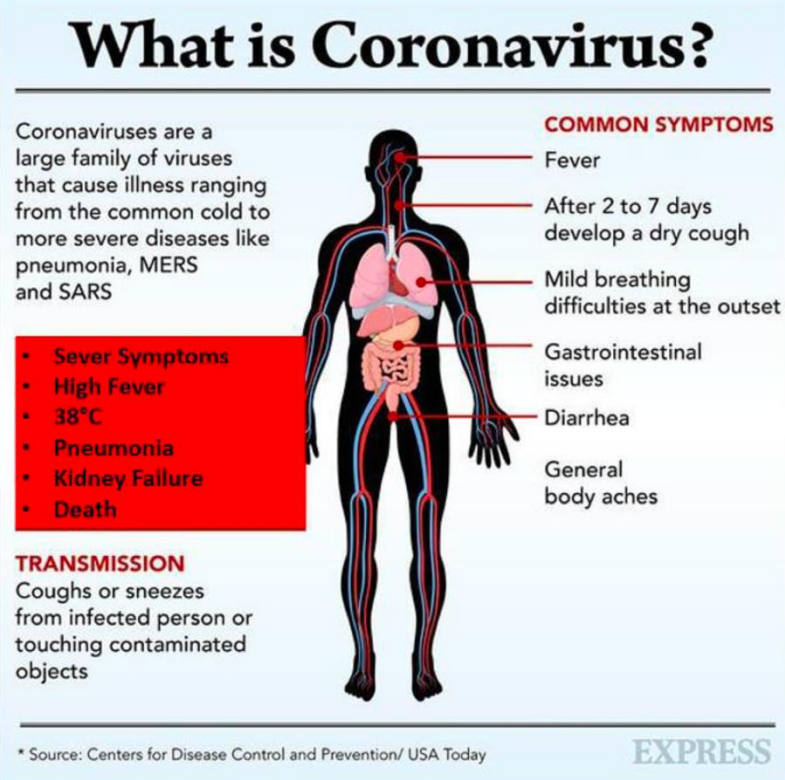
SARS-CoV-2 is a betacoronavirus closely related to SARS-CoV and MERS-CoV. It is an enveloped, non-segmented, positive sense RNA virus[5]. It is thought to have originated in bats but the animal that mediated transmission to humans remains unknown.

2.1 Epidemiology

The mean incubation period for COVID-19 is estimated to be 4-5 days, with an interquartile range of 2-7 days[6, 7]. Transmission from asymptomatic patients has now been proven to occur, but the extent of this is unknown[8]. The reproductive number for the virus is approximately 2.2-2.5, but may be as high as 3.6 early in the course of epidemics[6]. In early reported cases, the median age of patients was 50 years with a male preponderance (~60%), however areas with widespread population testing have shown high rates of asymptomatic or minimally symptomatic infection in younger adults. Very few severe cases which required hospitalisation have been reported among children under the age of 15 years (~1%), although school closures may have influenced this figure. Risk factors for severe disease include older age and cardiopulmonary comorbidities[7].

2.2 Clinical characteristics – what to look for

Figure 1: Common symptoms of COVID-19



80% of symptomatic patients develop mild disease, an estimated 15% develop severe disease (with hypoxaemia, dyspnoea and tachypnoea) while 5% become critically ill (with respiratory failure, septic shock and/or multiorgan dysfunction)[9]. The proportion of asymptomatic carriers is currently unknown.

The most common presenting symptom has been fever (~90%, but only present in 44% on admission). Other common symptoms include cough (68%), fatigue (38%), sputum production (34%), shortness of breath (19%), myalgia or arthralgia (15%), sore throat (14%), headache (13.6%) and chills (12%)[4].

Gastrointestinal symptoms also occur such as nausea, vomiting and diarrhoea in up to 10% of patients. Recent experience in Europe suggests that loss of taste and smell can also occur.

Abnormalities are visible on chest X-ray in ~60% of COVID-19 patients, and on ~85% of chest CT scans. Both are more common with severe disease (77% and 95% respectively). Radiological abnormalities may be apparent before PCR becomes positive[10, 11].

2.3 Outcomes and prognosis

The vast majority of cases will make a full recovery, though this may take several weeks, particularly in severe cases. In a minority of cases, COVID-19 has been associated with rapid progression to acute respiratory distress syndrome (ARDS), multiple organ failure and sometimes death. The true case fatality rate is currently unknown but is estimated to be within the range of 0.5-4%. Among the critically ill, mortality is attributed to respiratory failure, secondary bacterial infections with multi-drug resistant organisms, sepsis and shock[4].

3. Screening and triage

3.1 Case Definition and Early Identification

Patients fulfilling the latest case definition for suspected COVID-19 should be identified as soon as possible upon entering a health facility, to avoid prolonged contact with other patients and healthcare workers. Please see Table 1 for the Botswana case definitions which are adapted from NICD and WHO[1, 12] and Figure 3 for a summary.

Case and contact definitions are regularly revised as new information becomes available. When definitions specific to Botswana are revised, these will be published online and in regular situation reports.

Table 1: The Botswana case definitions, as of 28th April 2020, adapted from NICD and WHO[1, 12]

SUSPECTED CASE
1. A patient with acute respiratory illness (sudden onset of at least one of the following: cough, sore throat, shortness of breath or fever) AND a history of any travel outside of Botswana or to a location within Botswana reporting community transmission* of COVID-19 during the 14 days prior to symptom onset; OR 2. A patient with any acute respiratory illness (sudden onset of at least one of the following: cough, sore throat, shortness of breath or fever) AND having been in contact with a suspected, probable or confirmed case of COVID-19 (see definition of contact) in the last 14 days prior to symptom onset; OR 3. A patient who is hospitalised with a severe acute respiratory illness (sudden onset of at least one of the following: cough, sore throat, shortness of breath or fever) AND in the absence of an alternative diagnosis that fully explains the clinical presentation.
PROBABLE CASE
1. A suspect case for whom testing for the COVID-19 virus is reported by the laboratory as inconclusive. OR 2. A suspect 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.

CONTACT
A close contact is a person who experienced any one of the following exposures during the 4 days before and the 14 days after the onset of symptoms of a probable or confirmed case: 1. Face-to-face contact with a suspected, probable or confirmed case within 2 metres and for more than 15 minutes; 2. Direct physical contact with a suspected, probable or confirmed case; 3. In a closed environment (e.g. household, classroom, meeting room, hospital waiting room) with a COVID-19 case for more than 15 minutes; 4. Direct care for a patient with suspected, probable or confirmed COVID-19 disease without using proper personal protective equipment; 5. In the same hospital room when aerosol generating procedure is undertaken on a probable or confirmed COVID-19 case without recommended PPE; 6. In an aircraft or any other mode of conveyance sitting within two seats (in any direction) of a suspected, probable or confirmed COVID-19 case, travel companions or persons providing care, and crew members serving in the section of the aircraft where a COVID-19 case was seated. A casual contact is a person who experienced any one of the following exposures during the 4 days before and the 14 days after the onset of symptoms of a probable or confirmed case: 1. Face-to-face contact with a suspected, probable or confirmed COVID-19 case within 2 metres for less than 15 minutes; 2. In a in a closed environment with a COVID-19 case for less than 15 minutes. Note: for confirmed asymptomatic cases, the period of contact is measured as the 4 days before through the 14 days after the date on which the sample was taken which led to confirmation.

*Locations within Botswana reporting community transmission of COVID-19 will change as the epidemic evolves. Updates will be provided by the Ministry of Health and Wellness. At present, given the uncertain epidemiology of COVID-19 transmission in Botswana, all regions are considered to have possible community transmission.

ALL SUSPECTED CASES MUST BE NOTIFIED IMMEDIATELY TO THE DHMT SO THAT RAPID CONTACT TRACING CAN TAKE PLACE TO STOP ONWARD TRANSMISSION OF COVID-19. SEE GUIDELINE 6: CONTACT TRACING FOR MORE DETAIL.

3.2 Triage

All healthcare facilities need to prepare for the arrival of suspected COVID cases. This requires careful planning of services to minimise the number of patients attending and to restructure the way services are delivered.

All services need to adopt a triage system to screen patients for COVID-19.

Figure 2: WHO recommended approach for preparing a healthcare facility for COVID-19[13]

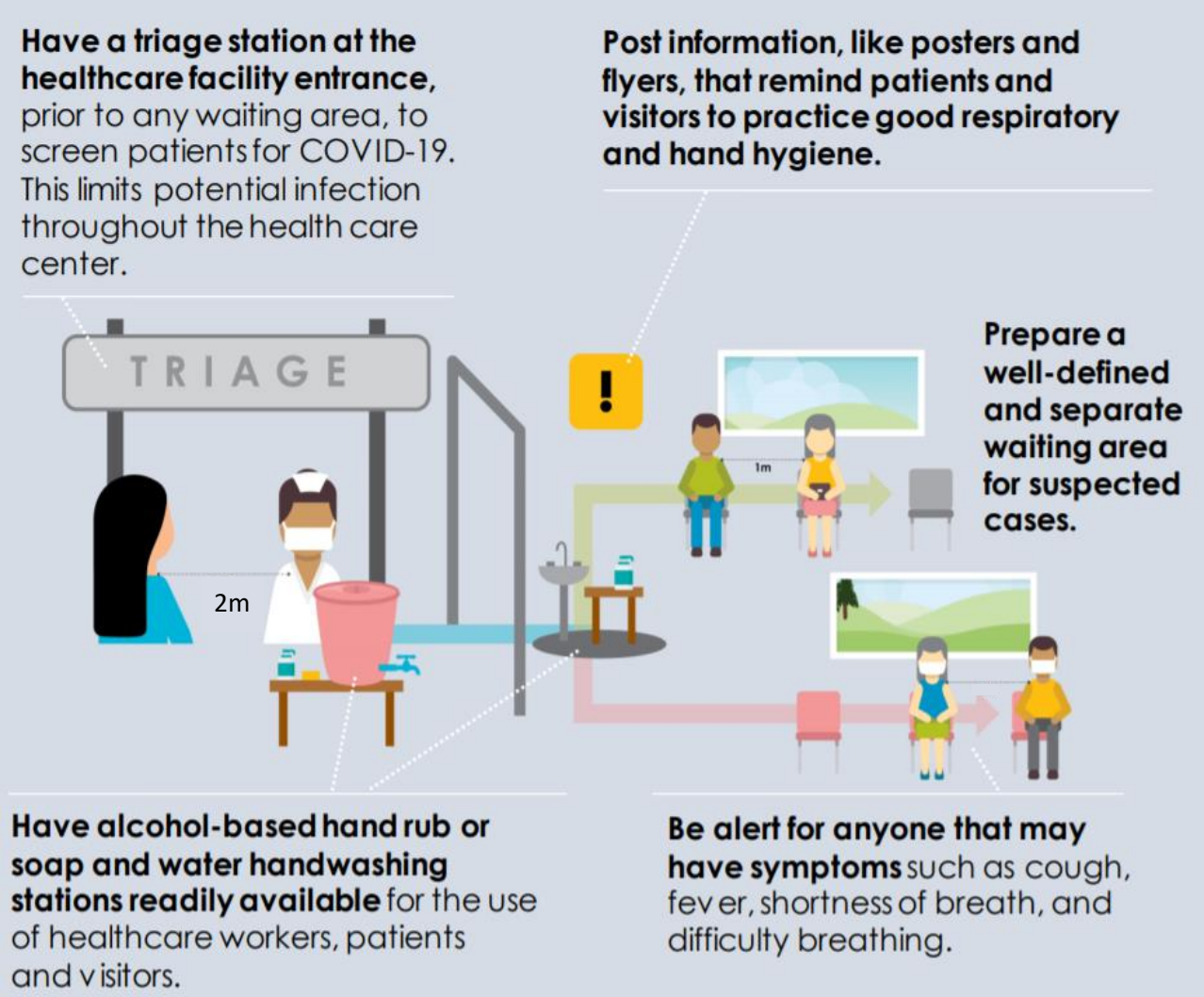
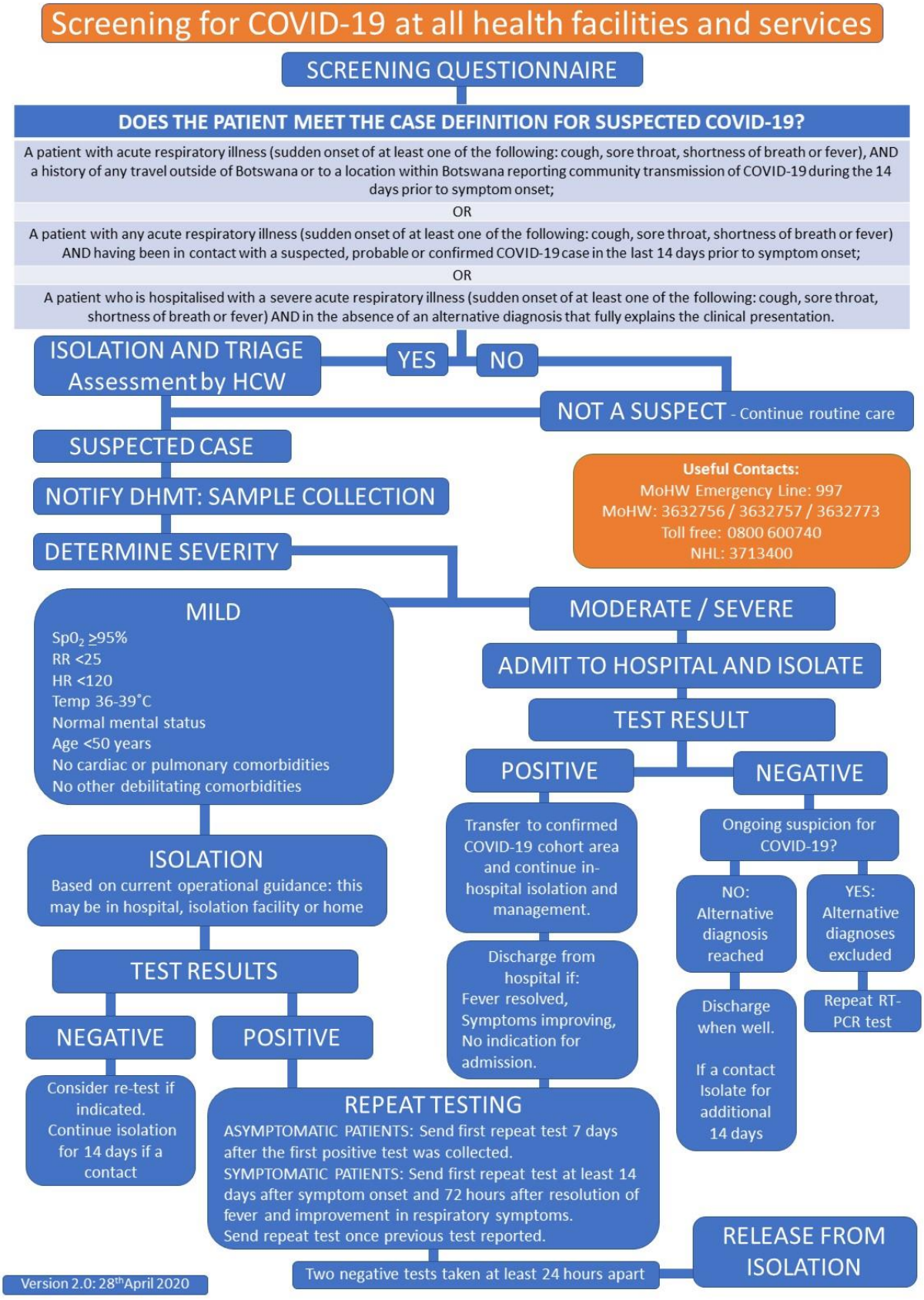


Figure 3: Algorithm for triaging patients with suspected COVID-19



3.3 Infection Control Measures

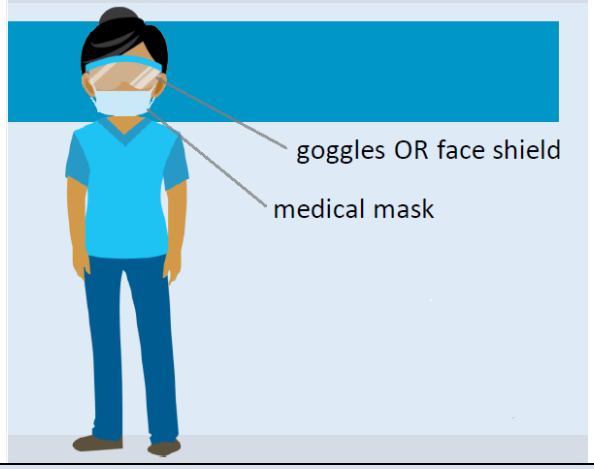
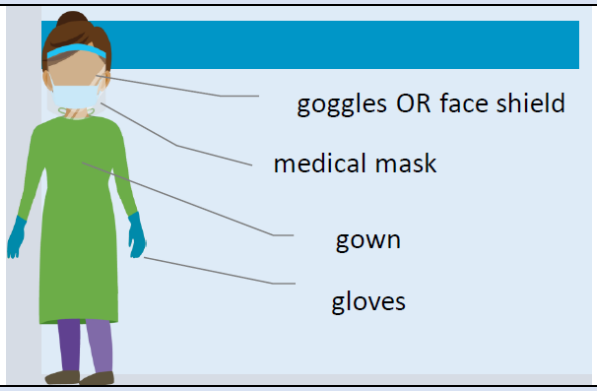
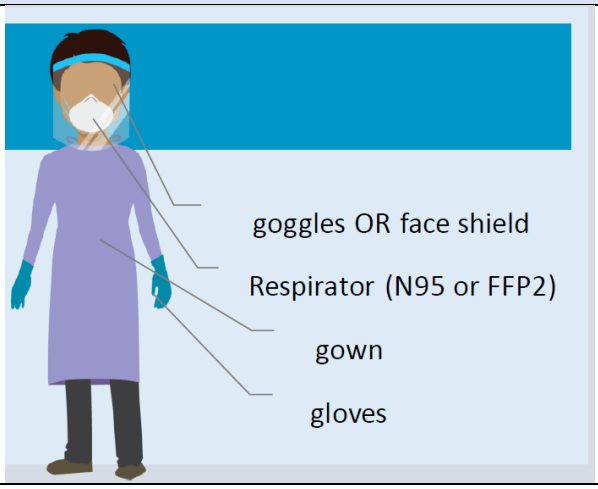
Table 2: Key infection control measures for COVID-19

AT SCREENING AND TRIAGE
• Give suspect patient a surgical mask. • Direct them to a separate isolation area. • Maintain a 2m distance between suspected patients and other patients. • Instruct all patients to cover nose and mouth with a flexed elbow or tissue when coughing or sneezing. • All staff and patients to perform regular hand hygiene at moments including; before and after touching another person; before engaging in clean/aseptic procedures; after body fluid exposure; after touching patient surroundings.
COHORTING
Allocate separate clinical space and group patients as follows: 1. Confirmed COVID-19 2. Suspected COVID-19 3. General patients who have screened negative for COVID-19
SUSPECTED CASES
• Place patients in single rooms, or group those together with other suspected COVID-19 cases. • Minimise the number of people in the room, including healthcare staff and relatives. • Ensure adequate room ventilation and keep windows open. • Healthcare workers to wear a surgical mask, goggles, gown and eye protection. • Continue to maintain a distance from the patient and minimise contact. • Disinfect stethoscopes and other clinical equipment. • Limit patient movement and ensure that patients wear surgical masks. • Disinfect rooms after use.
SAMPLE COLLECTION FOR COVID-19 TESTING
• If your facility cannot collect samples for COVID-19 testing, liaise with DHMT to facilitate sample collection and testing. • If your facility does collect samples for COVID-19 testing, please see sample collection guidelines below.
AEROSOL GENERATING PROCEDURES
• These include suction of chest secretions, bronchoscopy, intubation, extubation, cardiopulmonary resuscitation and the second stage of labour. • Use negative pressure rooms whenever possible with a minimum of 12 air changes per hour or at least 160 litres/second/patient in facilities with natural ventilation. • Wear a fit-tested particulate respirator (N95/FFP2), goggles, gloves and a long-sleeve gown • Avoid the presence of unnecessary individuals and try not to transfer patients.

3.4 Personal Protective Equipment

Personal protective equipment (PPE) stocks are limited and therefore PPE should be used rationally. Note that if a surgical mask is not available, a respirator mask can be used in its place. Refer to Guideline 2: Personal Protective Equipment for further detail.

Table 3: Recommended personal protective equipment for healthcare workers[13]

PATIENT SCREENING AND TRIAGE

COLLECTING RESPIRATORY SAMPLES, CARING FOR OR TRANSPORTING A SUSPECTED OR CONFIRMED CASE

CARING FOR A SUSPECTED OR CONFIRMED CASE USING AEROSOLISED PROCEDURES


4. Testing

4.1 Principles of testing

All suspected cases of COVID-19 need to undergo sample collection for testing.

Samples to be sent are:

- *Upper respiratory tract samples* – nasopharyngeal and oropharyngeal swabs (combined in the same universal transport medium tube) in all patients.
- *Lower respiratory tract samples* – if possible, send sputum, tracheal aspirates, or bronchoalveolar lavage fluid. Sputum induction is not recommended.

Samples are sent for Real Time RT-PCR. Please note that this is qualitative, not quantitative.

The sensitivity of the test is 70-80% so you are expected to encounter patients who have COVID-19 but test negative. In cases where you obtain a negative test but are strongly suspicious of COVID-19 please send a repeat sample[11].

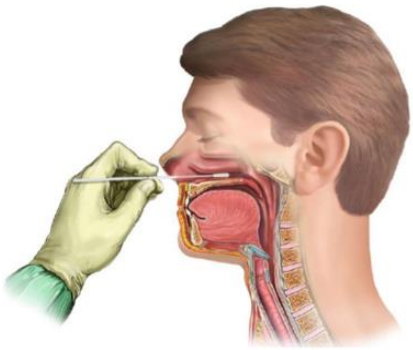
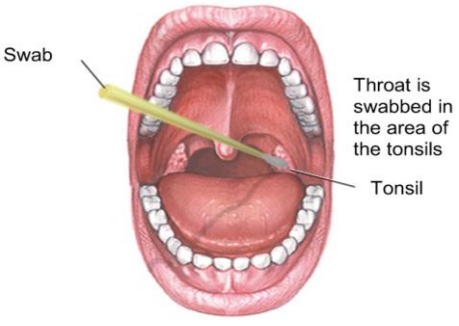
Imaging may strongly suggest that someone has COVID-19 or may be helpful to exclude other diagnoses. For example, pleural effusions, masses, cavitation and lymphadenopathy are all rare in COVID-19[10, 11].

Chest X-ray classically shows diffuse infiltrates which are predominantly peripheral and basal.

CT scan shows patchy ground glass opacities in the same distribution.

4.2 How to collect an upper respiratory tract sample

Table 4: How to collect an upper respiratory tract sample

EQUIPMENT REQUIRED	
• Specimen submission form • Nasopharyngeal (NP) and oropharyngeal (OP) flocked swabs: do not use cotton swabs • Tube containing universal transport medium (UTM) with patient's details written on in advance • Tongue depressor • Gloves, a surgical mask, eye protection and a gown • Biohazard bag for disposal of non-sharp materials. • Tissue for patient to wipe their nose after sample collection • Cooler box and cooled ice packs • Biopack for shipping	
OBTAINING A NASOPHARYNGEAL SWAB	
• Put on (don) PPE • Open a sterile dacron/polyester flocked swab at the plastic shaft • Ask the patient to tilt their head back. Estimate the distance from the patient's nose to the ear: this is how far the swab should be inserted • Insert the swab into the nostril and back (not upwards) until slight resistance is met • Rotate swab 2-3 times over 10-15 seconds • If resistance is met, try with another nostril • Slowly withdraw swab and put into specified transport medium • Break plastic shaft at break point and close the tube	
OBTAINING AN OROPHARYNGEAL SWAB	
• Keep the same gloves on and take a second swab • Ask the patient to tilt their head back and open their mouth wide • Hold the tongue down with a depressor and ask them to say 'aah' • Swab each tonsil and then the posterior pharynx in a figure 8 movement • Avoid the soft palate and tongue to avoid a gag reflex • Place the swab into the same tube and break the plastic shaft at the break point	
COMPLETING THE PROCESS	
• Tightly close the tube • Place the closed tube in the Biopack or in a cooler box with cooled ice packs • Multiple samples can be stored together • Take off (doff) PPE • Wash hands with soap and water • Arrange transport to testing facility	

4.3 Additional tests to consider

The differential diagnosis of suspected cases includes influenza, both conventional and atypical bacterial pneumonias, TB, and in patients with HIV and a CD4 count <200 cells/μL (or equivalent immunosuppression), Pneumocystis jirovecii pneumonia.

Depending on the patient, appropriate additional diagnostic and prognostic tests may include:

- Full blood count and differential
- Electrolytes, liver and kidney function tests
- CRP, LDH and D-dimer
- HIV test, CD4 cell count and viral load
- Blood cultures
- Arterial blood gases
- Nasopharyngeal swabs or aspirates and oropharyngeal swabs for detection of viral and atypical pathogens
- Sputum for MC+S and GeneXpert MTB/RIF Ultra
- Chest radiography (X-ray, ultrasound and/or CT scan)
- Urinary Legionella antigen
- Urine dipstick and culture
- Electrocardiogram

5. Management of suspected and confirmed COVID-19 Cases

The goal in clinical management of cases is to reduce morbidity and mortality and minimise transmission to uninfected contacts. Triaging patients and early identification of patients who are severely or critically ill and require hospital or ICU admission will be essential in reducing morbidity and mortality while isolation and implementation of infection prevention and control (IPC) measures within facilities as well as contact tracing, education on good cough hygiene and IPC at isolation facilities will help minimise onward transmission of the virus. Key management principles include:

5.1 Rapid triage of cases

Triage of suspected and confirmed cases requires an assessment to determine the severity of the illness. The following definitions should be used[14].

Mild illness

Patients with 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, dyspnoea, nasal congestion, or headache. Rarely, patients may also present with diarrhoea, nausea and vomiting. The elderly and immunosuppressed may present with atypical symptoms. Symptoms due to physiologic adaptations of pregnancy or adverse pregnancy events, such as e.g. dyspnoea, fever, GI-symptoms or fatigue, may overlap with COVID-19 symptoms.

Pneumonia

Adult with pneumonia but no signs of severe pneumonia and no need for supplemental oxygen.

Severe pneumonia

Adolescent or adult: fever or suspected respiratory infection, plus one of: respiratory rate > 30 breaths/min; severe respiratory distress; or SpO2 ≤ 93% on room air.

Acute respiratory distress syndrome

Onset: within 1 week of a known clinical insult 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.

Blood gases can be helpful to determine severity i.e. PaO_2/FiO_2 ratio.

In order that appropriate IPC measures and an appropriate level of supportive care can be commenced.

- Cases triaged as having moderate or severe disease will always require admission for medical reasons. Provided capacity exists, hospitals designated to manage COVID-19 cases should be primarily used for admissions.
- Patients with mild disease may be considered for management in an isolation facility or home isolation, dependent upon current operational guidance, and provided they are able to do this safely (see criteria in Table 5 below).
- If patients are to be managed at isolation facility or home isolation, it is imperative that all appropriate measures are taken to prevent onward transmission of the disease to others.
- Note also that in 10-15% of cases, those patients assessed as having "mild" disease may continue to worsen over the course of a week or more and become severely ill. **Patients managed from an isolation facility or home isolation need to be closely monitored in case of any clinical deterioration.**

Table 5: Criteria for management at an isolation facility or home isolation (for age >12 years):

1. Mild disease as defined by ALL of the below:
a. $Sp0_2 \geq 95\%$ b. Respiratory rate <25 c. HR <120 d. Temperature 36-39°C e. Normal mental status
2. Able to safely isolate outside of hospital
a. Separate bedroom with private bathroom available b. Patient able to contact and return to healthcare facility if becomes unwell
3. Not at high risk of deterioration defined by ALL of the below:
a. Age <50 years b. No cardiac or pulmonary comorbidities c. No other debilitating comorbidities (e.g. cancer)

5.2 Early supportive therapy in hospitalised COVID-19 patients

Oxygen[14-16]

- Oxygen therapy is likely to be the single most effective supportive measure in COVID-19 patients overall.
- Give supplemental oxygen therapy immediately to patients with low oxygen saturation.
- Start oxygen therapy if the $Sp0_2$ falls below 90% in adults[15].
- Once commenced, aim for an $Sp0_2$ of 92-96%.
- Do not over oxygenate as this is associated with harm.
- Titrate oxygen therapy up and down to reach targets by means of nasal cannula, a simple face mask or a face mask with reservoir bag, as appropriate.

Table 6: Estimated fraction of inspired oxygen from variable oxygen delivery devices

		
Nasal cannula	Simple face mask	Face mask with reservoir bag
O_2 flow rate 1-5 L/min	O_2 flow rate 6-10 L/min	O_2 flow rate 10-15 L/min
Estimated FiO_2 0.25-0.40	Estimated FiO_2 0.4-0.6	Estimated FiO_2 0.60-0.95

Fluids[15]

- Use conservative fluid management in patients with SARI when there is no evidence of shock.
- Aggressive fluid resuscitation may lead to pulmonary oedema and worsen oxygenation.
- In resuscitation for septic shock in adults, give 250–500 mL crystalloid fluid (normal saline or Ringer's Lactate) as rapid bolus in first 15–30 minutes and reassess for signs of fluid overload after each bolus.

Vasoactive Agents[15]

- Aim for a mean arterial pressure of 60-65 mmHg.
- Only start vasopressors once confirming that patients are fluid replete.
- We suggest using norepinephrine as first line vasoactive agent. If unavailable we suggest using vasopressin or epinephrine.
- If signs of poor perfusion and cardiac dysfunction persist despite achieving MAP target with fluids and vasopressors, consider an inotrope such as dobutamine.

Antibiotics

- If clinical suspicion for co-infection exists, consider empirical antimicrobials to treat co-pathogens causing the syndrome.
- Treat suspected or confirmed pneumonia with:
    - Co-amoxiclav 625mg PO TDS or 1.2gram IV TDS for seven days

      AND
    - Azithromycin 500mg OD/IV for seven days

Specific therapies

- Ensure patients have thromboprophylaxis prescribed if not contraindicated (see Figure 4).
- Do not routinely give systemic corticosteroids for treatment of COVID-19 unless they are indicated for another reason[17, 18].
- There is no current evidence from RCTs to recommend any specific anti-nCoV treatment for patients with suspected or confirmed COVID-19 infection.
- Do not therefore give hydroxychloroquine or chloroquine to patients unless as part of a clinical trial.
- If pneumocystis pneumonia is strongly suspected start high dose CTX and steroids, if necessary.
- Consider a blood transfusion if the Hb < 70 g/L (7.0g/dL) in the absence of extenuating circumstances such as myocardial infarction, severe hypoxaemia or acute haemorrhage. Targeting higher Hb thresholds (>90-100 g/L) does not lead to better outcomes in patients with sepsis.

5.3 Management of hypoxemic respiratory failure and ARDS

Recognize severe hypoxemic respiratory failure when a patient with respiratory distress is failing standard oxygen therapy. Patients may continue to have increased work of breathing or hypoxemia (SpO_2 <90%, PaO_2 <60 mmHg [<8.0 kPa]) even when oxygen is delivered via a face mask with reservoir bag.

High-flow nasal oxygen (HFNO) or non-invasive ventilation (NIV) are not widely available and are not recommended for the treatment of COVID-19 in Botswana. Risks of NIV include delayed intubation, large tidal volumes, and injurious transpulmonary pressures. Limited data suggest a high failure rate when MERS patients receive NIV.

If a patient's SpO_2 is <90% and/or there is increased work of breathing despite high flow oxygen delivered by a face mask with reservoir bag then intubation may be indicated. In this situation please contact an intensive care physician and/or anaesthetist in a timely manner as emergency intubations pose a high risk for care providers and patients.

For intubated patients with ARDS use lung-protective ventilation strategies. Always consult an expert intensivist if possible. Detailed recommendations on mechanical ventilation strategies are beyond the scope of this guideline. Nonetheless, the general principles in patients with ARDS include[19]:

- Aim for an initial tidal volume of 6mg/kg.
- FiO_2 and PEEP are the main determinants of oxygenation when titrating ventilation settings.
- Tidal volume up to 8 ml/kg predicted body weight is allowed if undesirable side effects occur (e.g. dyssynchrony, pH <7.15).
- Use lower inspiratory pressures (plateau pressure <30 cmH2O).
- Hypercapnia is permitted if meeting the pH goal of 7.30-7.45.
- In adults with moderate or severe ARDS consider prone ventilation for 12-16 hours daily.
- In patients with moderate or severe ARDS, moderately higher PEEP instead of lower PEEP is suggested. Please consult ARDSnet.org FiO_2/PEEP tables for further guidance.
- The use of deep sedation may be required to control respiratory drive and achieve tidal volume targets. The goal for sedation should be to use opioids for analgesia and control of ventilation (i.e. fentanyl infusion or boluses) and to

use the minimum amount of sedation (i.e. midazolam or propofol) necessary to mitigate the emotional trauma of mechanical ventilation.

- In patients with moderate-severe ARDS (PaO2/FiO2 <150), neuromuscular blockade by continuous infusion should not be routinely used. Continuous neuromuscular blockade may still be considered in patients with ARDS in certain situations: ventilator dyssynchrony despite sedation, such that tidal volume limitation cannot be reliably achieved; or refractory hypoxemia or hypercapnia.
- In settings with access to expertise in extracorporeal life support (ECLS), consider referral of patients with refractory hypoxemia despite lung protective ventilation.
- Avoid disconnecting the patient from the ventilator, which results in loss of PEEP and atelectasis. Use in-line catheters for airway suctioning and clamp endotracheal tube when disconnection is required (for example, transfer to a transport ventilator). HME filters are recommended to avoid droplet spread if circuit disconnect occurs and when manual bag ventilation is necessary.

Please also follow the guidance below to minimise adverse outcomes related to ventilation:

- Use weaning protocols that include daily assessment for readiness to breathe spontaneously.
- Minimise continuous or intermittent sedation, targeting specific titration endpoints (light sedation unless contraindicated) or with daily interruption of continuous sedative infusions.
- Oral intubation is preferable to nasal intubation in adults and adolescents.
- Keep patients in a semi-recumbent position (head of bed elevation 30-45°).
- Use a closed suctioning system, periodically drain and discard condensate intubing.
- Use a new ventilator circuit for each patient, once a patient is ventilated, change circuit if it is soiled or damaged but not routinely.
- Change head moisture exchanger when it malfunctions, when soiled, or every 5-7 days.
- Use venous thromboembolism prophylaxis – either low-molecular weight heparin or heparin if not contraindicated. For those with contraindications, use mechanical prophylaxis.
- Review urinary catheters on a daily basis.

- Turn patients every two hours.
- Give early enteral nutrition (within 48 hours of admission).
- Administer histamine-2 receptor blockers or proton-pump inhibitors

See Figure 5 for a clinical care summary.

Figure 4: VTE and anticoagulation considerations in admitted COVID-19 cases.

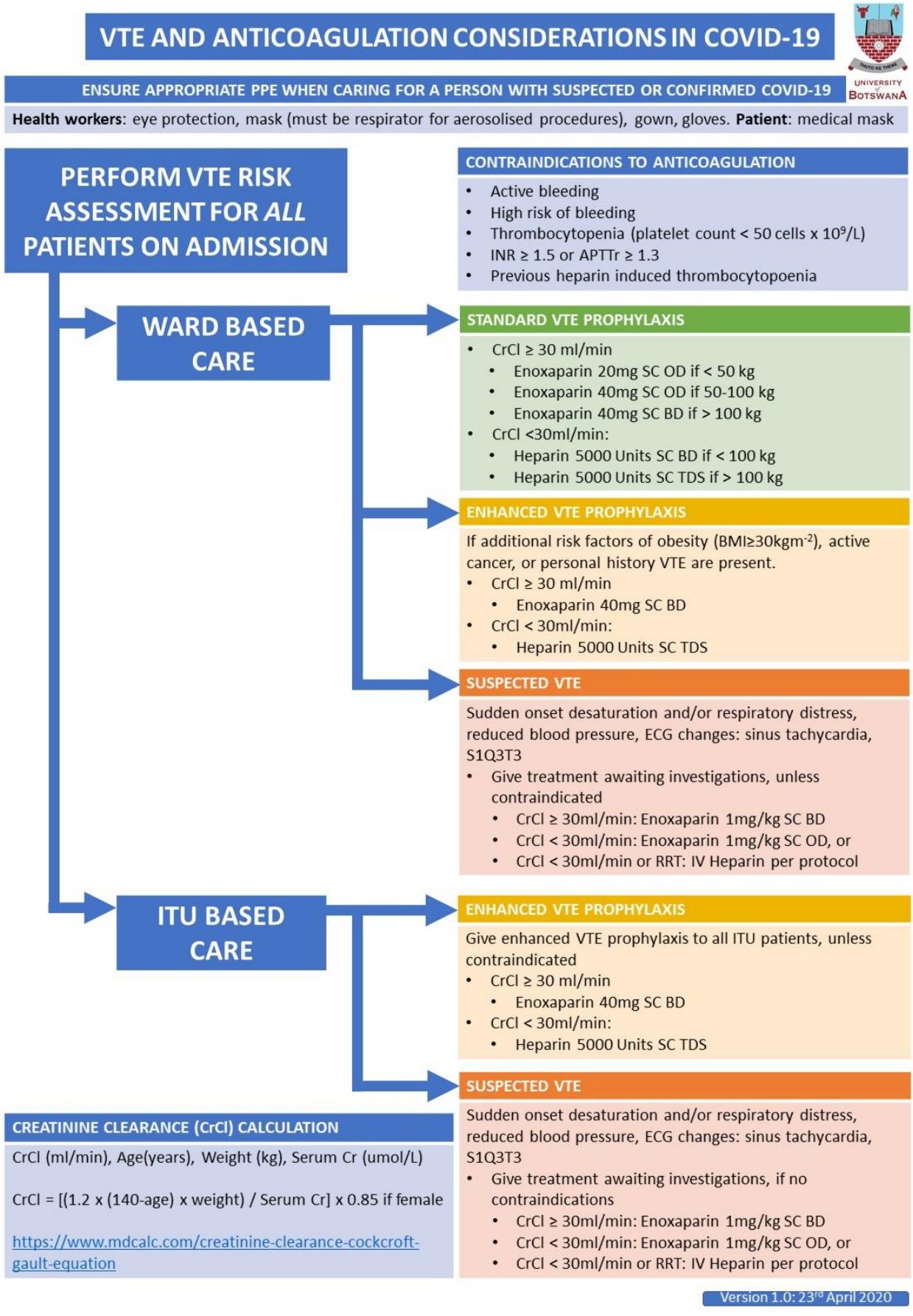


Figure 5: Clinical Care Summary

MANAGEMENT OF COVID-19 IN HOSPITAL

UNIVERSITY of BOTSWANA

ENSURE APPROPRIATE PPE WHEN CARING FOR A PERSON WITH SUSPECTED OR CONFIRMED COVID-19

Health workers: eye protection, mask (must be respirator for aerosolised procedures), gown, gloves. **Patient**: medical mask

INDICATIONS FOR ADMISSION

- SpO_2 <95%
- RR ≥25
- HR ≥120
- Temp >39˚C
- Abnormal mental status
- High risk for deterioration:
  - Age >50 years
  - Cardiac or pulmonary comorbidities
  - Other debilitating comorbidities

INITIAL INVESTIGATIONS

- Nasopharyngeal + oropharyngeal swabs and sputum for RT-PCR (see testing summary)
- Bloods: FBC and differential, urea, creatinine and electrolytes, liver function, CRP, coagulation
- Blood cultures
- ECG
- CXR

Consider:

- LDH, D-dimer, ferritin
- HIV test, CD4, VL
- Arterial blood gas
- Nasopharyngeal and oropharyngeal swabs for viral and atypical pathogens
- Urine dipstick and culture
- Sputum MC&S and GeneXpert MTB/RIF Ultra
- Additional radiology (CT, ultrasound)

INVESTIGATIONS – WHAT TO EXPECT

- Leukopenia and lymphopenia
- Mild thrombocytopenia
- Mildly elevated AST/ALT
- Elevated LDH and CRP
- CXR: ground glass opacities, typically peripheral and basal. Pleural effusion is uncommon
- Radiological changes may occur despite negative RT-PCR
- THINK non-COVID or co-infection: other pathologies with similar symptoms or presentation

ESTIMATED FIO_2 FROM VARIABLE OXYGEN DELIVERY DEVICES



O_2 flow rate 1-5 L/min	O_2 flow rate 6-10 L/min	O_2 flow rate 10-15 L/min
Estimated FiO_2 0.25-0.40	Estimated FiO_2 0.4-0.6	Estimated FiO_2 0.60-0.95

SUPPORTIVE CARE

- On admission, decide a treatment escalation plan
- Supplemental oxygen
  - Start oxygen if SpO_2 < 90% (or <92% if pregnant)
  - Titrate to target SpO_2 92-96%.
- Conservative use of IV fluids – only for dehydration with inadequate oral intake, or shock.
- Consider empirical antibiotics
  - Co-amoxiclav 625mg PO TDS / 1.2g IV TDS for 7 days
  - AND Azithromycin 500mg OD for 7 days
- Manage comorbidities
- Target Hb > 7.0 g/dL

AVOID

- Do not start steroids unless indicated for another reason
- Do not stop/start NSAID/ACEI/ARB unless otherwise indicated

VENOUS THROMBOEMBOLISM

- Perform VTE risk assessment for all patients
  - Enoxaparin 20mg SC OD if <50kg
  - Enoxaparin 40mg SC OD if 50-100kg
  - Enoxaparin 40mg SC BD if >100kg, or if additional risk factors of obesity (BMI≥30kgm^{-2}), active cancer, personal history VTE, or ITU admission.
  - CrCl <30ml/min: Heparin 5000 Units SC BD if <100kg
  - CrCl <30ml/min: Heparin 5000 Units SC TDS if >100kg, or if additional risk factors (as stated above), or ITU admission.
- Contraindications: PLT <50, INR >1.5, APTTr ≥ 1.3, active or high risk of bleeding, previous heparin induced thrombocytopoenia

Suspicion for PE

- Sudden onset desaturation and/or respiratory distress, reduced blood pressure, ECG changes: sinus tachycardia, S1Q3T3
- Wells Score, D-dimer, CTPA and/or Echo, if possible
- Treatment:
  - CrCl ≥ 30ml/min: Enoxaparin 1mg/kg SC BD
  - CrCl < 30ml/min: Enoxaparin 1mg/kg SC OD, or
  - CrCl < 30ml/min or RRT: IV Heparin per protocol

RECOGNISE DETERIORATION

- Failing maximal standard O_2 therapy
  - Increased work of breathing
  - Exhaustion
  - SpO_2<90% despite 40% facemask O2
  - Inability to protect airway
- Refer for intubation and ventilation early

PRINCIPLES OF INTENSIVE CARE MANAGEMENT

- Norepinephrine preferred vasoactive agent.
- Target MAP 60-65mmHg
- Mechanical ventilation
- Low tidal volume 4-8ml/kg
- Target plateau pressures <30cm
- Higher PEEP (≥10cmH20)
- Consider prone ventilation

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5.4 Discharge from hospital

The decision to discharge a patient with confirmed COVID-19 from hospital is a medical one which is made by the clinician caring for the patient. Patients with confirmed COVID-19 can be discharged from hospital providing:

- Their fever has resolved.
- Their symptoms are improving.
- There is no other indication for admission.
- They can be discharged to an isolation facility (or home isolation depending on current operational guidance) OR they can be safely released from isolation (see below) and discharged home (see Section 6 for de-isolation criteria).

Patients who are admitted with suspected COVID-19 and managed in a suspected cohort area but test negative for COVID-19 can be discharged from hospital providing:

- Their fever has resolved.
- Their symptoms are improving.
- There is no other indication for admission.

All patients who have been admitted to a suspected COVID-19 area who are discharged are to then be treated as contacts of COVID-19 and must remain in facility or home isolation for a further 14 days after discharge.

6. Release from isolation (de-isolation)

Some patients may be well enough to be discharged from hospital but still need to remain in isolation until they meet the below de-isolation criteria. These individuals may continue to be isolated at a facility or at home, dependent upon current operational guidance. For more information please refer to Guideline 5: Quarantine and Isolation.

6.1 De-isolation criteria

Patients with confirmed COVID-19 can only be released from isolation (de-isolated) when they have two consecutive negative RT-PCR tests which were taken at least 24 hours apart. After receiving two consecutive negative tests the patient has recovered.

The approach to testing for recovery and de-isolation depends upon whether the patient was symptomatic with COVID-19.

Asymptomatic cases – Send first repeat test 7 days after the first positive test was collected.

Symptomatic cases – Send first repeat test at least 14 days after symptom onset and 72 hours after resolution of fever and improvement in respiratory symptoms (whichever is later).

On the day that a repeat test is reported, send another test that same day and continue this process until two negative results are received.

When a patient is de-isolated they are able to return home (if not already isolating at home) but are advised to minimise contact with other people for a further 14 days.

6.2 Facility isolation after hospital discharge

Patients who are clinically stable but who have not yet had two negative RT-PCR tests may be transferred to a designated isolation facility for ongoing isolation:

- Transfer must be via ambulance/EMS service.
- The receiving facility should be informed prior to the transfer of the patient.
- IPC guidance must be followed at all times. See SOP 1: Infection Prevention and Control for more detail
- The patient must remain in isolation until they meet the de-isolation criteria.
- Depending on current operational guidance, patients may be transferred from facility isolation to home isolation.

6.3 Home isolation after hospital discharge

Depending on current operational guidance, patients who are clinically stable but who have not yet had two negative RT-PCR tests may be transferred to their own home for ongoing isolation.

A trained healthcare worker must conduct a home assessment to verify whether the residential setting is suitable for providing care and assess whether the patient and family are capable of adhering to IPC guidance.

- Transfer home must be via ambulance/EMS service.
- The patient should be actively monitored by a healthcare worker through home visits or telephone follow-up.
- IPC guidance must be followed at all times.
- The patient must remain in isolation until they meet the de-isolation criteria.

6.4 Recovery

There is no internationally accepted consensus definition of "recovery" from COVID-19 for reporting purposes. Given this, at present Botswana will report patients as having "recovered" when they are de-isolated according to the criteria above, i.e. clinically stable for at least 72 hours and two negative RT-PCR tests on nasopharyngeal swabs taken 24 hours apart. This may subject to change as the epidemic progresses.

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