Republic Of Namibia

MANAGEMENT OF CONFIRMED COVID-19 CASES
STANDARD OPERATING PROCEDURES: NAMIBIA

Date: 5 April 2020. Version 1.5

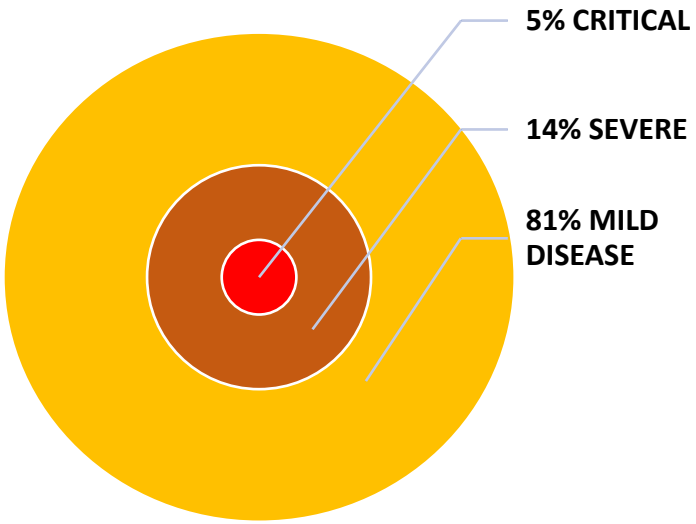
This SOP is being constantly updated as new information is available and providers should always ensure that they are using the most up to date guideline version.

Introduction

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.

Patients with confirmed COVID-19 who need hospitalization can be managed at either state or private hospitals depending on where the patient presented. This is to minimize referrals which further expose more healthcare workers to COVID-19.

According to WHO, about 81% of patients with COVID-19 may have mild disease; 14% of patients will have severe disease that requires oxygen therapy or other inpatient interventions; and about 5% have critical disease that requires mechanical ventilation.



High Risk Populations

Age above 60 years old
Smoker
Cardiovascular disease
Diabetes
Poorly controlled hypertension
Immune deficiency states including HIV
Pre-existing pulmonary disease
Chronic disease such as chronic kidney disease and Chronic Respiratory disease

Mild Disease Criteria:

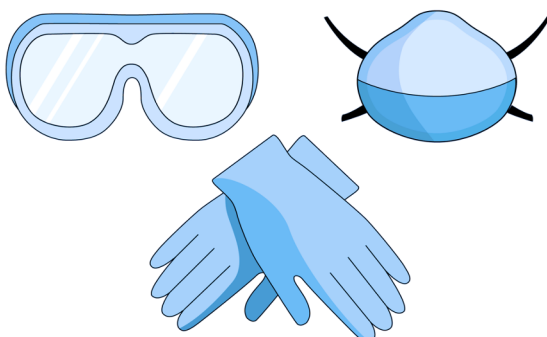
Adults
SpO2 ≥95%
Respiratory rate <25
HR <120
Temp 36-39°C
Normal mental status

Children 5 -12
Respiratory rate < 30
HR < 130

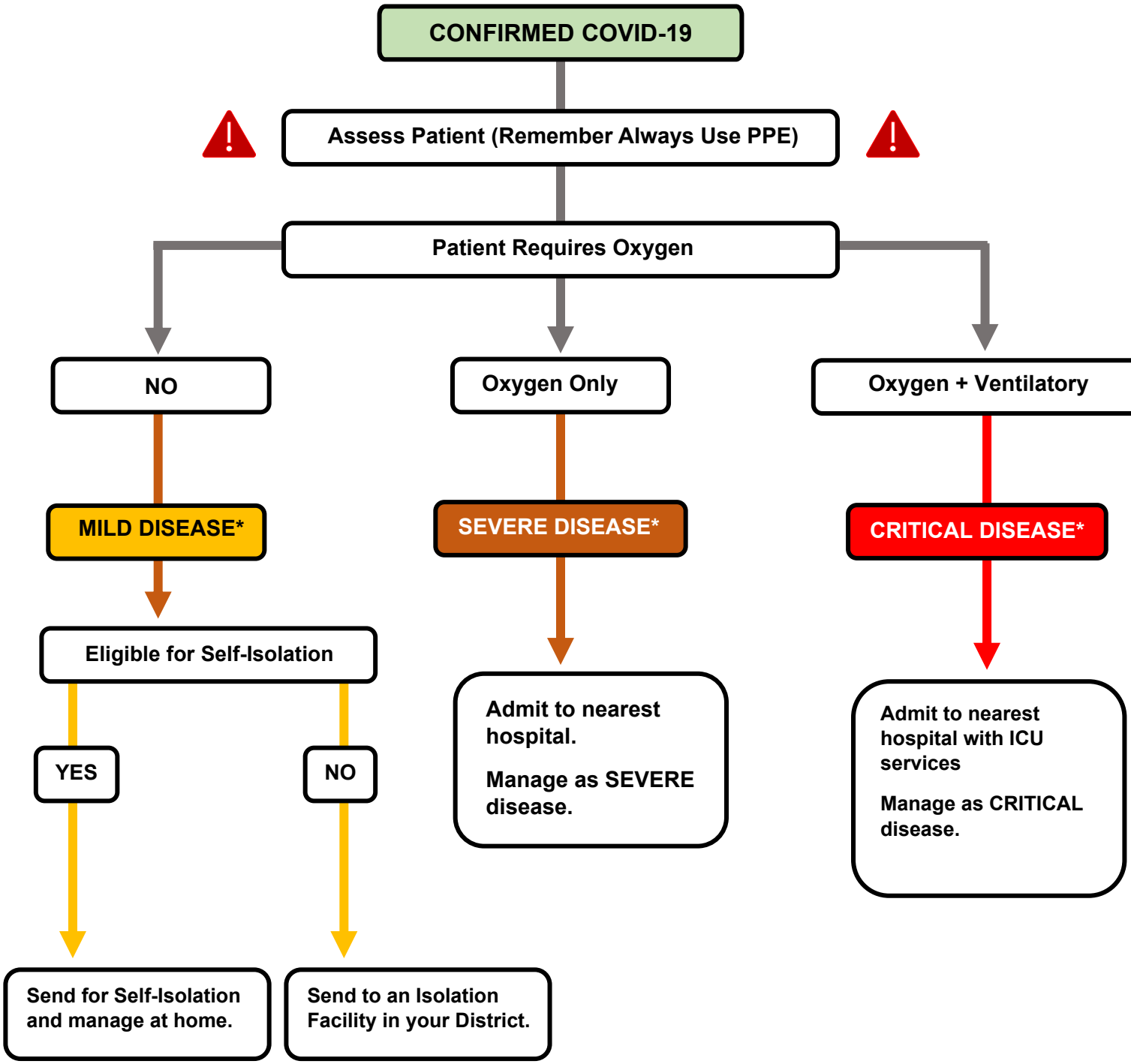
Severe and Critical

Severe – Requires oxygen
Critical – Requires ventilatory support
Present with severe respiratory distress to failure
Multi-organ failure

ALWAYS WEAR PPE



MANAGEMENT OF CONFIRMED COVID-19 CASE



Deisolation and Discharge Criteria

- There are no medical indications for admission.
- The patient's symptoms have improved or resolved. (Note: full recovery can take several weeks, especially in severe cases. It is not necessary for every symptom to have completely resolved prior to discharge, only that there has been improvement).
- The patient has two consecutive negative combined nasopharyngeal and oropharyngeal RT-PCR tests performed at least 24-48 hours apart.

***See criteria for use of Hydroxychloroquine**
In Namibia, both State and Private health facilities are able to manage confirmed COVID cases.

Management of Mild Cases

- Patients with asymptomatic or mild disease may be considered for management at home, provided they are able to safely self-isolate and are not at risk of developing severe disease.
- If patients are to be managed at home, it is imperative that all appropriate measures are taken to prevent onward transmission of the disease to others.
- Provide patients with mild disease with symptomatic treatment such as antipyretics for fever.
- 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 home need to be given the contact details of their doctor or healthcare facility that they can reach out to in case of any clinical deterioration.**

Criteria for Self-isolation at Home

Able to Safely Self-isolate:

- Separate bedroom available for patient to self-isolate in for 14 days.
- Separate bathroom and toilet for patient to use, not used by anyone else.
- Contacts in the house should not be above age of 50 years.
- Patient able to contact the toll-free number 0800 100 100, and return to, healthcare facility in case of deterioration
- No cardiac or pulmonary comorbidities
- No other debilitating comorbidities (e.g. cancer, diabetes, autoimmune diseases etc.)

Steps to Take During Self-isolation:

- **Stay at home for the entire period of self-isolation**.
- Do not use public transport or taxis when going to health care facilities.
- Minimize time you spend in shared spaces like living rooms & kitchen. Wear a mask when in shared spaces with other people. Keep a minimum distance of 1 meter between yourself and others when in common spaces.
- Do not share utensils and crockery.
- Keep the rooms well ventilated by opening windows to allow in fresh air.
- Monitor your health and body temperature. Take your temperature twice a day in the morning and evening and at any other time you think you may have a fever. Record the readings in the log provided by MOHSS.
- If your clinical condition deteriorates during this period, contact MOHSS/hotline clinic immediately on 0800-100-100.

Self-care Guidelines for Self-isolation:

- Set a healthy daily routine for yourself. Keep well hydrated and maintain regular mealtimes and exercise times.
- Keep yourself busy with in-house activities you enjoy.
- Set a time limit of exposure to media updates on COVID-19 to avoid triggers of worry and agitation.
- Seek support and encouragement from friends &, family through phone, email, social media or skype.
- Avoid unhealthy coping mechanisms to deal with your emotions (e.g. smoking, drinking or use of other drugs)

- If you live alone plan how you to access your food/groceries and other required supplies by asking assistance from friends and family. They can purchase the supplies and leave them outside the door for collection. You can also consider using online shopping applications for home delivery of supplies in similar fashion.
- Keep in contact with hotline 0800 100 100 for important health advice or to receive timely treatment if required.
- The MOHSS counselors, are on hand on the hotline 0800 100 100 to offer support together with the network of other counselors.

Patients with COVID-19 can be de-isolated provided they meet ALL of the following criteria:

1. There are no medical indications for admission.
2. The patient's symptoms have improved or resolved. (Note: full recovery can take several weeks, especially in severe cases. It is not necessary for every symptom to have completely resolved prior to discharge, only that there has been improvement).
3. The patient has two consecutive negative combined nasopharyngeal and oropharyngeal RT-PCR tests performed at least 24-48 hours apart.

Management of Severe COVID-19

Patients with severe COVID-19 require urgent care with oxygen therapy. These patients will require hospitalization.

Oxygen therapy and monitoring

- Give supplemental oxygen therapy immediately to patients with SARI and respiratory distress, hypoxaemia or shock and target > 94% and ≥ 92–95% in pregnant patients.
- Closely monitor patients with COVID-19 for signs of clinical deterioration, such as rapidly progressive respiratory failure and sepsis and respond immediately with supportive care interventions.
- Application of timely, effective and safe supportive therapies is the cornerstone of therapy for patients that develop severe manifestations of COVID-19.
- Understand the patient's co-morbid condition(s) to tailor the management of critical illness.
- Monitor for drug-drug interactions.
- Use conservative fluid management in patients with SARI when there is no evidence of shock.

Treatment of co-infections

- Give empiric antimicrobials to treat all likely pathogens causing SARI and sepsis as soon as possible, within 1 hour of initial patient assessment for patients with sepsis.
- Empiric therapy should be de-escalated based on microbiology results and clinical judgment.

Management of Critical COVID-19

Acute Respiratory Distress Syndrome (ARDS)

- Recognize severe hypoxemic respiratory failure when a patient with respiratory distress is failing standard oxygen therapy and prepare to provide advanced oxygen/ventilatory support.
- Endotracheal intubation should be performed by a trained and experienced provider using airborne precautions.
- Rapid sequence intubation is appropriate after an airway assessment that identifies no signs of difficult intubation.

For intubated patients with ARDS use lung-protective ventilation strategies

- Aim for an initial tidal volume of 6mg/kg.16 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).16
- Hypercapnia is permitted if meeting the pH goal of 7.30-7.45.
- Application of prone ventilation >12 hours a day is strongly recommended for patients with pressures.
- In patients with moderate or severe ARDS, moderately higher PEEP instead of lower PEEP is 16 targets.
- In patients with moderate-severe ARDS (PaO2/FiO2 <150), neuromuscular blockade by continuous infusion should not be routinely used.

Septic Shock

- Recognize septic shock in adults when infection is suspected or confirmed AND vasopressors are needed to maintain mean arterial pressure (MAP) ≥ 65 mmHg AND lactate is ≥ 2 mmol/L, in absence of hypovolemia.
- Recognize septic shock in children with any hypotension (systolic blood pressure [SBP] < 5th centile or > 2 SD below normal for age) or two or more 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 pulses; tachypnoea; mottled or cold skin or petechial or purpuric rash
    - Increased lactate; oliguria; hyperthermia or hypothermia.

Special Populations

Pregnant women with COVID-19

- Considering asymptomatic transmission of COVID-19 may be possible in pregnant or recently pregnant women, as with the general population all women with epidemiologic history of contact should be carefully monitored.
- Pregnant women with a suspected, probable or confirmed COVID-19 infection, including women who may need to spend time in isolation with obstetric, foetal medicine and neonatal care, as well as mental health and psychosocial support, with readiness to care for maternal and neonatal complications.
- Currently no evidence that pregnant women present with increased risk of severe illness or fetal compromise.
- Pregnant and recently pregnant women who have recovered from COVID-19 should be enabled and encouraged to attend routine antenatal or postpartum care as appropriate.

Infants and Mothers with COVID-19

- Infants born to mothers with suspected, probable or confirmed COVID-19 infection, should be fed according to standard infant feeding guidelines, while applying necessary precautions for IPC.

- As with all confirmed or suspected COVID-19 cases, symptomatic mothers who are breastfeeding or practicing skin-to-skin contact or kangaroo mother care should practise 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.

- Breastfeeding counselling, basic psychosocial support and practical feeding support should be provided to all pregnant women and mothers with infants and young children, whether they or their infants and young children have suspected or confirmed COVID-19.

- In situations when severe illness in a mother due to COVID-19 or other complications prevent her from caring for her infant or prevent her from continuing direct breastfeeding, mothers should be encouraged and supported to express milk, and safely provide breastmilk to the infant, while applying appropriate IPC measures

Monitoring of Patients

Patients may continue to be PCR positive after clinical resolution, although for how long such virus is viable (and thus infectious) remains to be determined. Repeat nasopharyngeal and oropharyngeal swabs should be only be sent once the patient's fever (if present) has resolved, clinical improvement has been noted, and a minimum of 7 days has passed since the initial positive test. Samples should be sent every 2 days until two consecutive negative RT-PCR tests have been documented.

DO Repeat RT PCR once:
7 days after initial positive test
AND
Fever resolved
AND
Symptoms improving or resolved

DO this until **2 consecutive Negative** RT PCR tests 48hrs apart.

Discharge and Deisolation Criteria

Patients with COVID-19 can be discharged home provided the meet ALL the following criteria:

1. There are no medical indications for admission.
2. The patient's symptoms have improved or resolved. (Note: full recovery can take several weeks, especially in severe cases. It is not necessary for every symptom to have completely resolved prior to discharge, only that there has been improvement).
3. The patient has two consecutive negative combined nasopharyngeal and oropharyngeal RT-PCR tests performed at least 24-48 hours apart.

Patients with mild disease who were managed at home from the outset can be deisolated using the same criteria.

Drugs and Information

Use of Hydroxychloroquine

Mechanism of action: Heme polymerase inhibitor; increases the pH of the phagolysosome, which interrupts virus/cell fusion, as well as interferes with the glycosylation of cellular receptors of SARS-CoV2.

Evidence Summary: Hydroxychloroquine has been shown to inhibit replication of SARS-CoV2 in vitro (Wang et al, 2020). Chloroquine has been shown to inhibit many viruses *in vitro*. However, it has not been shown to be an effective antiviral *in vivo* in limited trials. In an animal model of chikungnya virus infection, chloroquine delayed the immune response, resulting in lack of viral clearance (Reviewed in Touret & deLamballerie, 2020). In a recently published open-label, non-randomized study, of 20 patients with COVID-19 who received hydroxychloroquine 200 mg three times daily 14 (70 %) had clearance of virus from the nasopharynx at day 6, compared to 2 (12.5%) of 16 who did not receive hydroxychloroquine (p= 0.001) (Gautret et al, 2020 in press).

Administration

AGENT	DOSAGE	REMARKS	MAIN TOXICITIES
Hydroxychloroquine Pro-drug of chloroquine available in 200 mg tablets	400mg PO bid x 1 day, then 200mg PO bid x 4 days No dosing adjustment for renal or hepatic impairment or obesity Pharmacy can compound suspension if requested Chloroquine phosphate 500 mg PO q12h for 10 days, equivalent to 300mg chloroquine base)	Safe in pregnancy Metabolized by CYP2C8, CYP3A4 and lesser extent CYP2D6 ~20-30% excreted unchanged in urine. Anuric patient steady state levels are ~30% higher than patients w/ normal renal function	Most toxicities are associated with long-term use; Dizziness, headache, loss of appetite, nausea, vomiting LFT abnormalities QTc prolonging effects; monitor QTc – see monitoring guidance below

Eligibility Criteria In Namibia:

1. All confirmed health care workers.
2. Mild cases with risk factors
3. All severe and critical cases.

LOPINAVIR/RITONAVIR

Lopinavir/ritonavir is a fixed-dose combination antiretroviral for treatment of HIV infection. Both drugs are protease inhibitors; ritonavir slows lopinavir metabolism (boosts lopinavir). This medication is hypothesized to inhibit SARS-CoV-2-encoded protease; however, inhibitory lopinavir levels exceed achievable blood levels.

Evidence Summary: In vitro activity against SARS-CoV2, retrospective trial in patients with SARS.

Improved outcomes when used as initial treatment compared to matched cohort (2.3% death vs 15.6%), no difference in outcomes when used as rescue therapy. (Chan 2003). In a randomized, open-label study of lopinavir-ritonavir 400-100 mg BID x 14 days vs. placebo for treatment of COVID-19 were enrolled in China (ChiCTR2000029308). The primary endpoint was time to clinical improvement, secondary endpoints included 28 day mortality and detectable RNA levels during therapy. 199 patients with laboratory documented SARS-CoV-2 infection and evidence of impaired oxygenation (O2 sat≤94% or PaO2:FiO2<300 mm Hg) were enrolled. There was no difference in primary or secondary outcomes.

Based on these data, lopinavir-ritonavir is **not recommended.**

Corticosteroids

Data on the use of corticosteroids for novel coronavirus infections are quite variable with mixed results and little clarity on appropriate dosing or timing. In SARS-CoV, any steroid therapy was associated with increased need for ICU admission or mortality, although lower mortality and shorter hospitalization was seen among critical cases and pulse steroids did

appear to result in lower oxygen requirements and better radiographic outcomes compared to non-pulsed steroids. In MERS-CoV, however, steroid therapy was evaluated both by dose and duration and no effect was seen on mortality; however, increased time to viral clearance was observed. One study of SARS-CoV-2 suggests, delayed use of steroids may increase risk of death in the ICU. In another COVID-19 cohort, the use of methylprednisolone in patients who developed ARDS was associated with decreased risk of death; short courses of low-moderate dose steroids have also been recommended in critically ill patients. Given these mixed data, and the potential for steroid therapy to worsen disease severity and lead to secondary infections, routine use of steroids is not recommended at this time.

Use of steroids in patients with severe disease (requiring oxygen support or mechanical ventilation) could be considered as part of the supportive care regimen for patients with ARDS on a case-by-case basis.

Non-Steroidal Anti-inflammatory Drugs (NSAIDs)

No evidence exists to support its use in mitigating the inflammatory response associated with COVID-19. There have been concerns voiced regarding clinical worsening of COVID-19 in patients taking ibuprofen but these are unsubstantiated at this time. **We do not recommend NSAIDS primarily due to lack of evidence for benefit.** These drugs can also exacerbate acute kidney injury in the setting of serious illness.

Angiotensin-receptor blockers and Angiotensin converting enzyme blockers

SARS-CoV-2 uses ACE2 receptor for cell entry in the lungs and thus the course of the infection could be impacted by the use of these antihypertensive agents. Furthermore, ACE2 itself is protective against lung injury, thus reduced levels may exacerbate pulmonary complications. There is no consensus on whether these drugs would exacerbate or ameliorate COVID-19 disease. No clinical data currently exist to guide the initiation or cessation of these agents in patients with SARS-CoV19 infection. The HFSA, ACC and AHA emphasize the lack of experimental or clinical data on these class of drugs in COVID-19 and recommend that patients currently taking these medications for known beneficial indications (HF, HTN, or ischemic heart disease, for example) be advised to continue them. They advise against adding/removing beyond what would be done in standard practice and urge individualized treatment decisions based on patient's clinical presentation and haemodynamic. Ongoing clinical trials, including of recombinant ACE2, are currently underway.