NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
Division in the National Health Laboratory Service

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

CLINICAL MANAGEMENT OF SUSPECTED OR CONFIRMED COVID-19 DISEASE

Version 2 (19th March 2020)

Contents

Writing committee (in alphabetical order): David Anderson, Tom Boyles, Lucille Blumberg, Cheryl Cohen, Ahmad Haeri Mazanderani, Tendesayi Kufa-Chakeza, Halima Dawood, Fikile Mabena, Shaheen Mehtar, Patrick Moonasar, Natalie Mayet, Marc Mendelson, Jeremy Nel, Jantjie Taljaard

Version 2: What's New?

- New guidance on treatment options for hospitalized cases (section 4.3)
- New de-isolation criteria for confirmed cases (section 4.5)
- Statement on the use of ACE-inhibitors, angiotensin receptor blockers, and nonsteroidal anti-inflammatory drugs (section 4.3).

Guideline Summary

Testing

- Apply the latest case definition from the NICD to determine testing eligibility. http://www.nicd.ac.za/diseases-a-z-index/covid-19/
- Combined nasopharyngeal and oropharyngeal swabs should be sent in all suspected cases. Lower respiratory tract samples (e.g. sputum) can also be sent if present (do not perform sputum induction however).
- Ensure that the specimen is labelled and packaged correctly, and stays between 2-8°C during specimen storage and transport.

Suspected COVID-19 cases

- Any suspected case should be identified as soon as possible (ideally prior to entering the facility). Such cases should immediately be given a surgical mask, and be isolated. Good hand hygiene and cough etiquette should be taught, and appropriate samples obtained.
- A broad differential diagnosis should be entertained for suspected cases, and appropriate testing for alternative diagnoses should be undertaken.
- Suspected COVID-19 cases who are medically well, or who are assessed as having only mild disease, may be managed at home while awaiting test results.

Confirmed COVID-19 cases

- Patients with 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 (see criteria in table 2).
- Supportive oxygen therapy is the cornerstone of management for patients with severe disease – target oxygen saturations of ≥90% for most patients, using nasal prong oxygen, a simple face mask, or a face mask with a reservoir bag.
- For intubated patients with ARDS, use lung-protective ventilation strategies.
- Although there is currently no good evidence for any specific therapy for COVID-19, consider chloroquine for cases requiring hospitalization, as well as for mild cases who have risk factors for severe disease.
- Patients may be de-isolated without the need for repeat PCR tests. Those with mild disease may be de-isolated 14 days after symptom onset, while those with severe disease may be de-isolated 14 days after achieving clinical stability (e.g. once supplemental oxygen is discontinued).
- There is currently no good evidence to suggest that patients on ACE-inhibitors, angiotensin-receptor blockers need to discontinue these agents.

Healthcare worker personal protective equipment (PPE)

- For the majority of COVID-19 patient interactions, appropriate healthcare worker PPE consists of gloves, a gown or apron, and/or a surgical mask.
- When performing aerosol-generating procedures (e.g. taking nasopharyngeal swabs, performing CPR, or intubating a patient), an N95 respirator should be used in place of a surgical mask, and eye protection (shield or goggles) should be added to the above.

Clinical management of suspected or confirmed COVID-19 disease

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. 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. These guidelines describe the clinical management of cases 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.

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. 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.[2,3] Transmission from asymptomatic patients has been postulated, but the extent of this is unknown.[4] The reproductive number for the virus is approximately 2.2.[2] In the early reported cases, the median age of reported cases was 50 years with a male preponderance of cases (~60%). 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.

2.2 Clinical characteristics – what to look for

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).[5] 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%).[3] Gastrointestinal symptoms such as nausea or vomiting (5.0%) and diarrhoea (3.8%) appear to be uncommon.

Abnormalities are visible on chest X-ray in ~60% of COVID-19 patients, and on ~85% of patients' chest CT scans. Both are more common with severe disease (77% and 95% respectively).[3]

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 case fatality ratio is currently unknown, but is estimated to be within the range of 0.5-4%.

3. Management of Suspected COVID-19 Cases

3.1 Early identification/triage

Patients fulfilling the latest case definition for suspected COVID-19 case (a "person under investigation") should be identified as soon as possible upon entering a health facility, to avoid prolonged contact with other patients and healthcare workers.

- The criteria for a "person under investigation" (PUI) are dynamic and will change with time. For the latest criteria, please see the NICD's website: http://www.nicd.ac.za/diseases-a-z-index/covid-19/
  As of 19th March 2020, the case NICD's case definition is:

> Persons with acute respiratory illness with sudden onset of at least one of the following: cough, sore throat, shortness of breath or fever [≥ 38°C (measured) or history of fever (subjective)] irrespective of admission status
>
> **AND**
>
> In the 14 days prior to onset of symptoms, met at least one of the following epidemiological criteria:
> - Were in close contact with a confirmed or probable case of SARS-CoV-2 infection;
>
> **OR**
> - Had a history of travel to areas with local transmission of SARS-CoV-2 (the list of these countries will change with time – consult the NICD website)
>
> **OR**
> - Worked in, or attended a health care facility where patients with SARS-CoV-2 infections were being treated
>
> **OR**
> - Admitted with severe pneumonia of unknown aetiology

- Measures that may facilitate the earliest possible identification of suspected COVID-19 cases include:
  - Posters, pamphlets, billboards or staff members outside and within the healthcare facility asking patients who fulfil criteria for a PUI to identify themselves to healthcare workers as soon as possible (rather than remaining in line in a waiting area).

    - Including a screening questionnaire for COVID-19 as part of the standard triage form at healthcare facilities.
- Any patient who fulfils criteria for a suspected COVID-19 case should immediately have the following measures taken:
    - Give the patient a medical (surgical) mask (N95 respirators are NOT required for patients).
    - Direct the patient to a separate area, preferably an isolation room if available. Where an individual isolation room is not available, a 1-2 metre distance should be kept between suspected COVID-19 cases and other patients.
    - Instruct the patient to cover his/her nose and mouth during coughing or sneezing with a tissue with a flexed elbow. The patient should perform hand hygiene after contact with respiratory secretions (wash hands or use alcohol-based hand rub, which should be readily available at the point of triage).
    - Limit the movement of the patient (e.g. use portable X-rays rather than sending the patient to the X-ray department). If the patient has to be moved, ensure that (s)he wears a mask.
    - The patient should have a dedicated bathroom (where this is possible).
- Patients should be quickly triaged in terms of clinical severity. Routine emergency department triage systems may be used. In the context of COVID-19, triaging is essential because:
    - It allows for rapid initiation of supportive therapy (e.g. oxygen supplementation)
    - It has implications for whether or not the patient can be allowed home to await results of the COVID-19 testing (see below).
    - It protects both patients and staff.

3.2 Testing

All persons under investigation require testing for SARS-CoV-2 by means of reverse transcriptase PCR (RT-PCR). Samples to be sent are:

- *Upper respiratory tract samples* – nasophargyngeal and oropharyngeal swabs (combined in the same universal transport medium tube) in all patients.
- *Lower respiratory tract samples* – may not be possible depending on the patient's symptoms. Where available, send sputum, tracheal aspirates, or bronchoalveolar lavage fluid. Sputum induction should not be performed.

Appropriate personal protective equipment (PPE) should be worn by all healthcare workers when obtaining specimens (see IPC section below).

The **differential diagnosis** of suspected cases includes influenza (remembering the seasonality in patients from the northern hemisphere differs from those of the southern hemisphere), both conventional and atypical bacterial pneumonias, and in patients with HIV and a CD4 count <200 cells/mm^3 (or equivalent immunosuppression), *Pneumocystis jirovecii* pneumonia. Depending on the patient, appropriate samples may include:

- Full blood count + differential count
- Blood cultures
- Nasopharyngeal swabs or aspirates and oropharyngeal swabs for detection of viral and atypical pathogens
- Chest radiography
- Urine *Legionella* antigen
- Sputum for MCS and/or *Mycobacterium tuberculosis* detection (GeneXpert MTB/RIF Ultra).
- Urine for lipoarabinomannan (LAM) test if HIV positive

Obtaining samples for SARS-CoV-2 testing

- Healthcare workers obtaining respiratory samples require appropriate personal protective equipment, including those for contact, droplet and aerosol precautions (see infection prevention and control section below).
- Collecting a good quality specimen is vital. For details on how to properly obtain good quality specimens, please see Appendix 5 of the NICD's COVID-19 guidelines for case-finding, diagnosis, management and public health response in South Africa: http://www.nicd.ac.za/wp-content/uploads/2020/02/Guidelines-for-case-finding-diagnosis-management-and-public-health-response-in-South-Africa.pdf

Transport of specimens

- Ensure that samples are kept between 2-8°C until they are processed.

For samples sent to the NICD:
Mark all samples as :

Suspected COVID-19 CRDM
NHLS/NICD
Centre for Respiratory Diseases and Meningitis (CRDM)
Lower North Wing, SAVP Building
1 Modderfontein Road, Sandringham, Johannesburg, 2131

NHLS laboratories use usual overnight region courier service. Private labs should organise shipment using existing systems, or contact CRDM for assistance if shipping is unavailable.

3.3 Empiric treatment of other pathogens

Where the patient fits the appropriate clinical syndrome, consider treatment of other pathogens such as:

- Conventional community-acquired pneumonia pathogens (or hospital-acquired pneumonia pathogens if appropriate) – e.g. amoxicillin-clavulante [see SA community-acquired pneumonia guidelines]

- Atypical pneumonia pathogens – e.g. azithromycin [see SA community-acquired pneumonia guidelines]
- Influenza (if influenza epidemiology fits and has severe illness or if patient is at risk of severe influenza) – oseltamivir [see NICD influenza guidelines]
- PJP (if appropriate risk factors present, e.g. HIV with low CD4 count)

3.4 Managing patients at home while awaiting COVID-19 test results

Suspected COVID-19 cases who are medically well, or who are assessed as having only mild disease, may be managed at home while awaiting test results.

Table 1 – Criteria for "mild" disease (for age >12 years)[1]

Criteria for "mild" disease
• SpO_2 ≥95% • Respiratory rate <25 • Heart rate <120 • Temp 36-39°C • Mental status normal

[1]For age 5-12, use respiratory rate <30, and heart rate <130. For younger ages, use age-appropriate normal values.

Such patients should be instructed to self-isolate at home and be given appropriate advice about reducing possible transmission to others:

- Patients should stay in a specific room and use their own bathroom (if possible). Patients should avoid unnecessary travel and unnecessary contact with other people.
- Where contact is unavoidable, the patient should wear a facemask, and maintain a distance of at least 1 metre (preferably 2 metres) from other people
- Patients should clean their hands with soap and water frequently. Alcohol-based sanitizers may also be used, provided they contain at least 70% alcohol.
- Patients should practice good cough and sneeze hygiene, by using a tissue, and then immediately discarding the tissue in a lined trash can, followed by washing hands immediately.
- Patients should not have visitors in their home. Only those who live in their home should be allowed to stay.
- At home, the patient should stay in a specific room and use his/her own bathroom (if possible). If they live in shared accommodation (university halls of residence or similar) with a communal kitchen, bathroom(s) and living area, they should stay in their room with the door closed, only coming out when necessary, wearing a facemask if they do so.
- Patients should avoid sharing household items like dishes, cups, eating utensils and towels. After using any of these, the items should be thoroughly washed with soap and hot water.
- All high-touch surfaces like table tops, counters, toilets, phones, computers, etc. should be appropriately and frequently cleaned.
- If patients need to wash laundry at home before the results are available, then they should wash all laundry at the highest temperature compatible for the fabric using laundry detergent. This should be above 60° C. If possible, they should tumble dry and iron using the highest setting compatible with the fabric. Disposable gloves and a plastic apron should be used when handling soiled materials if

possible and all surfaces and the area around the washing machine should be cleaned. Laundry should not be taken to a laundrette. The patient should wash his/her hands thoroughly with soap and water after handling dirty laundry (remove gloves first if used).

- Patients should know who to call if they develop any worsening symptoms, so that they can be safely reassessed.
- In addition to being given the above advice, a patient information sheet can be given if possible (see Appendix 1 for an example).

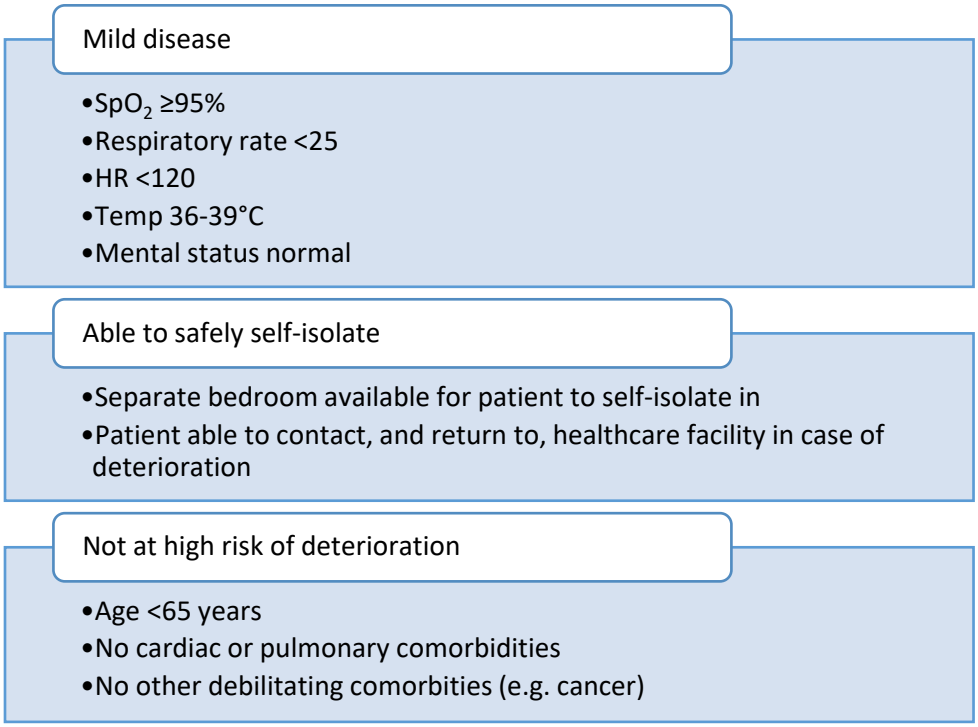
4. Management of Confirmed COVID-19 Cases

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 home will help minimise onward transmission of the virus. Key management principles include:

4.1 Rapid triage of cases – 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 require admission for medical reasons.
- Patients with 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 (see criteria in table 2).
- If patients are to be managed at home, is imperative that all appropriate measures are taken to prevent onward transmission of the disease to others - give advice as in section 3.1 above.
- 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.**
- Patients managed from home will have monitoring and subsequent viral sampling (see section 4.5) facilitated by their local health department. The NICD will alert each provincial health department of all new cases on a daily basis to facilitate this process.

Table 2 - Criteria for management at home (for age >12 years[1]):

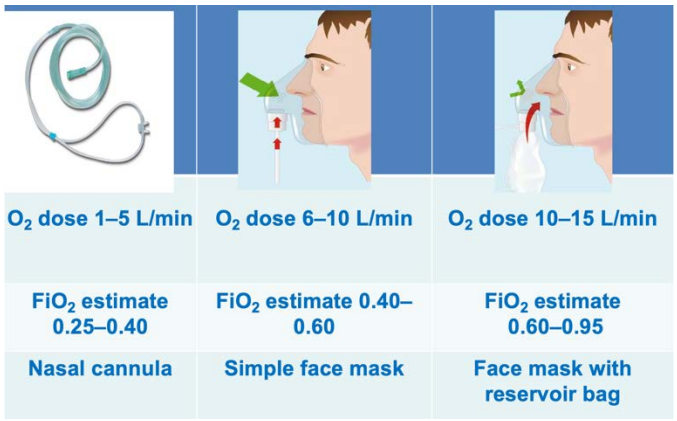


[1]For age 5-12, use respiratory rate <30, and heart rate <130. For younger ages, use age-appropriate normal values.

4.2 Early supportive therapy in hospitalised COVID-19 patients

Give supplemental oxygen therapy immediately to patients with low oxygen saturation.

- Oxygen therapy is likely to be the single most effective supportive measure in in COVID-19 patients overall. Target SpO_2 ≥90% in non-pregnant adults and SpO_2 ≥92-95 % in pregnant patients.[6] Children with emergency signs (obstructed or absent breathing, severe respiratory distress, central cyanosis, shock, coma or convulsions) should receive oxygen therapy during resuscitation to target SpO_2 ≥94%; otherwise, the target SpO_2 is ≥90%.
- 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:



O_2 dose 1–5 L/min	O_2 dose 6–10 L/min	O_2 dose 10–15 L/min
FiO_2 estimate 0.25–0.40	FiO_2 estimate 0.40–0.60	FiO_2 estimate 0.60–0.95
Nasal cannula	Simple face mask	Face mask with reservoir bag

Use conservative fluid management in patients with SARI when there is no evidence of shock. Aggressive fluid resuscitation may worsen oxygenation, especially in settings where there is limited availability of mechanical ventilation.[7,8]

If a clinical suspicion for co-infection exists, consider empiric antimicrobials to treat co-pathogens pathogens causing the syndrome, particularly in severe cases. This may include conventional and atypical bacterial pathogens, influenza and PJP (see section 3.3 above).

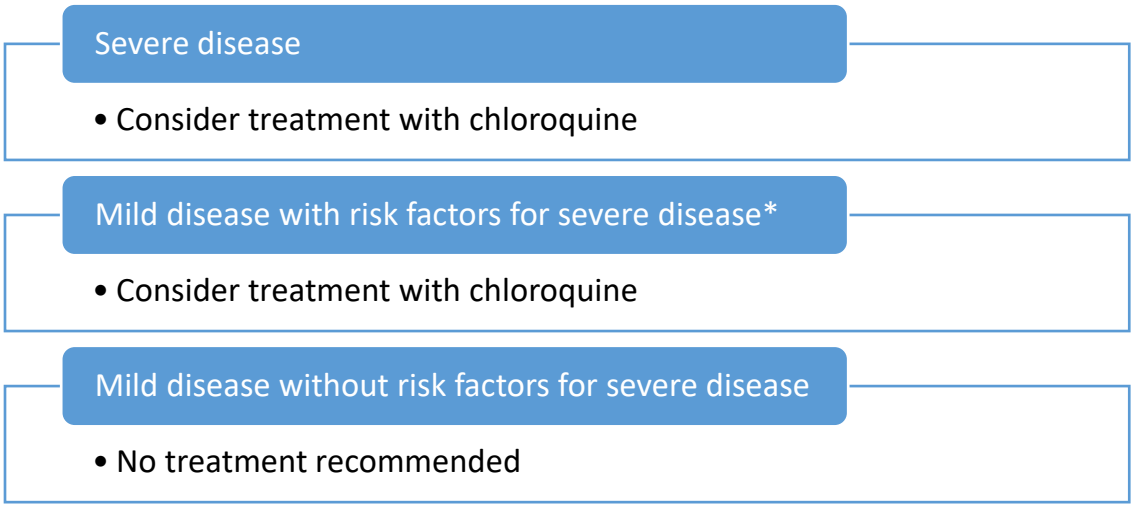
Closely monitor patients with SARI for signs of clinical deterioration, such as rapidly progressive respiratory failure and sepsis, and apply supportive care interventions immediately.

4.3 Specific therapies

Do not routinely give systemic corticosteroids for treatment of COVID-19 unless they are indicated for another reason.

A systematic review of observational studies of corticosteroids administered to patients with SARS reported no survival benefit and possible harms (avascular necrosis, psychosis, diabetes, and delayed viral clearance).[9] A systematic review of observational studies in influenza found a higher risk of mortality and secondary infections with corticosteroids; the evidence was judged as very low to low quality due to confounding by indication.[10] A subsequent study that addressed this limitation by adjusting for time-varying confounders found no effect on mortality.[11] Finally, a recent study of patients receiving corticosteroids for MERS used a similar statistical approach and found no effect of corticosteroids on mortality but delayed lower respiratory tract (LRT) clearance of MERS-CoV.[12] Given lack of effectiveness and possible harm, routine corticosteroids should be avoided unless they are indicated for another reason.

There is no current evidence from RCTs to recommend any specific treatment for patients with suspected or confirmed COVID-19 infection. This is an area of active study, however. Candidate drugs undergoing investigation include remdesivir, lopinavir/ritonavir, chloroquine, interferon, and toculizumab. To date, published clinical data on most of these agents consists largely of in vitro studies, with little or no human data. One exception is lopinavir/ritonavir, which was studied in a recent randomized control trial of patients with severe COVID-19.[13] No benefit was seen with respect to viral load, time to clinical improvement, or mortality. Given the state of evidence, the difficulties in procuring many of these agents in South Africa, and drug-drug interactions between chloroquine and lopinavir/ritonavir, we suggest consideration of the following:



*Risk factors for severe disease are age >65 years, or underlying cardiac or pulmonary disease

Drug	Suggested dosing regimen	Comment
Chloroquine	10mg/kg base daily for 2 days, then 5 mg/kg base daily for 1 day	Watch QTc, check for drug-drug interactions

Note:

- Where possible, consideration should be given to enroll hospitalized patients in clinical trials. This provides both monitoring and ethics oversight, as well as potentially affording the patients access to agents such as remdesivir.

There is no evidence for the use of any drug or vaccine to prevent COVID-19 infection. Prevention consists of non-pharmaceutical interventions, such as good hand hygiene and social distancing.

Statement on the use of angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARBs), and nonsteroidal anti-inflammatory drugs in COVID-19 patients

Recent work suggested that patients on ACEi or ARBs upregulate ACE2 receptors, the binding site for SARS-CoV-2, within tissues including the lung and heart, prompting concern that this might place patients at risk of worse outcomes with COVID-19.[1] For the moment, this remains purely theoretical, with no evidence of a linkage to poor clinical outcomes. In addition, discontinuing or switching ACEi or ARBs to alternative agents may be deleterious to patient care. **Pending further evidence we therefore do not recommend switching patients off ACEi or ARBs unless there are other medical reasons to do so.**

The evidence regarding nonsteroidal anti-inflammatory drugs (NSAIDs) in COVID-19 is similarly lacking. Nonetheless, where short-term fever or pain relief is required, it may be prudent to avoid this class of agents where possible. For patients requiring NSAIDs for chronic comorbidities, the evidence is not definitive enough to recommend discontinuation.

4.4 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. Hypoxemic respiratory failure in ARDS commonly results from intrapulmonary ventilation-perfusion mismatch or shunt and usually requires mechanical ventilation.

High-flow nasal oxygen (HFNO) or non-invasive ventilation (NIV) should only be used in selected patients with hypoxemic respiratory failure. The risk of treatment failure was high in patients with MERS treated with NIV, and patients treated with either HFNO or NIV should be closely monitored for clinical deterioration.

Patients with hypercapnia (exacerbation of obstructive lung disease, cardiogenic pulmonary oedema), hemodynamic instability, multi-organ failure, or abnormal mental status should generally not receive HFNO, although emerging data suggest that HFNO may be safe in patients with mild-moderate and non-worsening hypercapnia.[14] Patients receiving HFNO should be in a monitored setting and cared for by experienced personnel capable of endotracheal intubation in case the patient acutely deteriorates or does not improve after a short trial (about 1-2 hrs).

- 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.[12]
- Recent publications suggest that newer HFNO and NIV systems with good interface fitting do not create widespread dispersion of exhaled air and therefore should be associated with low risk of airborne transmission, though this is an area of ongoing study and so *airborne precautions should be used.*[15-17]

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 the guideline. Nonetheless, the general principles in patients with ARDS include:

- Aim for an initial tidal volume of 6mg/kg.[18] 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 cmH_2O).[18]
- 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 severe ARDS.[18]
- In patients with moderate or severe ARDS, moderately higher PEEP instead of lower PEEP is suggested.[18]
- The use of deep sedation may be required to control respiratory drive and achieve tidal volume targets.
- In patients with moderate-severe ARDS (PaO_2/FiO_2 <150), neuromuscular blockade by continuous infusion should not be routinely used.[19] Continuous neuromuscular blockade may still be considered in patients with ARDS in certain situations: ventilator dyssynchony despite sedation, such that tidal volume limitation cannot be reliably achieved; or refractory hypoxemia or hypercapnia.
- In settings with access to expertise in extracorporeal life support (ECLS), consider referral of patients with refractory hypoxemia despite lung protective ventilation.[20-22]
- 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).

4.5 De-isolation criteria

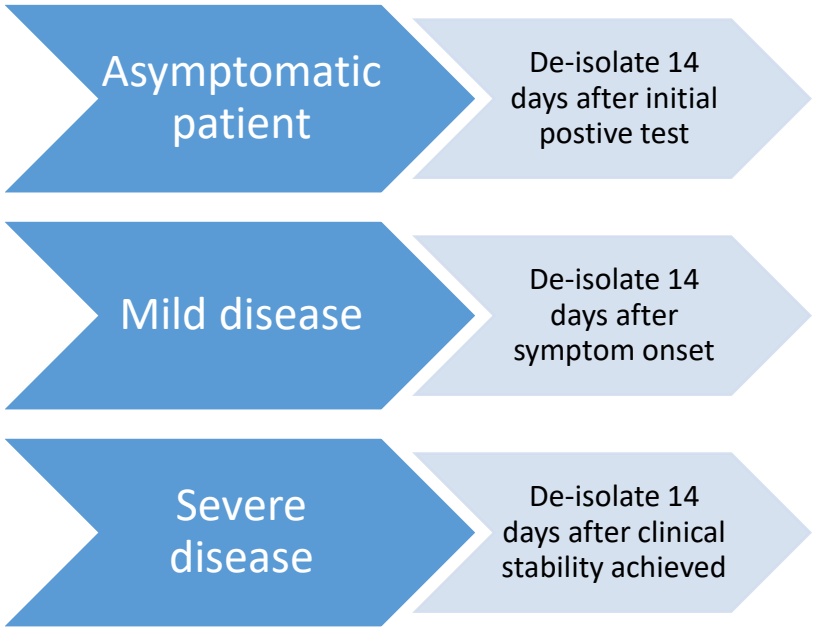
Patients can be de-isolated 14 days after the onset of their symptoms (mild cases), or 14 days after achieving clinical stability (moderate-severe cases).

Patients continue to shed SARS-CoV-2 from their upper airways for approximately 20 days (range 8-37 days), with mild cases showing viral shedding for a shorter period of time than severe cases.[23] However, viral shedding does not necessarily equate to infectiousness - viral shedding may decline to a level below the infectious threshold before it ceases completely, and/or non-viable virus may be shed. In a small cohort of mild COVID-19 cases managed in Germany, no virus was able to be cultured specimens from the upper or lower respiratory tract 8 days after symptom onset, despite the presence of detectable virus from these samples.[24] The probability of culturing live virus (indicating possible infectivity) was estimated to decline to <5% by day 10. Given the small sample size, we suggest de-isolating patients with mild disease 14 days after symptom onset.

Patients with severe disease (i.e. requiring admission due to clinical instability) may continue to shed virus at higher levels for longer periods. We therefore suggest de-isolating such patients 14 days after clinical stability has been achieved (e.g. after supplemental oxygen was discontinued).

Patients who remain asymptomatic after a positive COVID-19 result can be de-isolated 14 days after their positive test. Although asymptomatic patients might be expected to be less infectious than symptomatic patients, in one study the two groups' viral loads were shown to be similar, and we believe a similarly cautious approach to de-isolation is warranted.[23]

Patients admitted to hospital can continue their isolation period at home once clinical stability has been achieved, provided that the criteria in table 2 are met.



5. Infection prevention and control (IPC)

IPC is a critical and integral part of clinical management of patients and should be initiated at the point of entry of the patient to hospital (typically the Emergency Department). **A combination of standard, contact and droplet precautions should be practiced for all COVID-19 cases, and further precautions when performing aerosol-generating procedures (AGP).**

Standard precautions are used to prevent or minimize transmission of pathogens at all times, and should be applied to all patients in healthcare facilities irrespective of their diagnosis or status. These include hand hygiene, appropriate use of PPE, safe handling of sharps, linen and waste, disinfection of patient care articles, respiratory hygiene, occupational health and injection safety.

Transmission-based precautions - droplet, and contact:

- Hand hygiene is the first and most essential aspect
- Healthcare worker PPE consists of gloves, gown (or apron), and a medical mask.
- Safe waste management
- 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.
- Limit patient movement within the institution (e.g. where possible, use portable X-rays rather than sending the patient to the X-ray department), and ensure that patients wear medical masks when outside their rooms.

Aerosol-generating Procedures:

Aerosol precautions are required when performing aerosol-generating procedures. These include taking respiratory tract samples for SARS-CoV-2 testing (such as nasopharyngeal and oropharyngeal swabs), intubation, bronchoscopy, open suctioning of the respiratory tract, and cardiopulmonary resuscitation.
Aerosol precautions for healthcare workers:

- Healthcare worker PPE consists of gloves, gown (or apron), a fit-tested particulate respirator (N95 respirator), and eye protection (goggles or face shield).
- Use an adequately ventilated single room when performing aerosol-generating procedures, with spacing between beds of at least 1-1.5 metres.

For more details, refer to the World Health Organization IPC guidelines: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/infection-prevention-and-control

6. Recording and reporting

The goal of clinical management is to reduce morbidity and mortality from COVID-19 It is important to record and report the cases of COVID-19 disease in order to track the size and severity of the epidemic, the care received by patients in and out of hospital and identify areas for improvement in current and future outbreaks. There different tools which will be needed to record and report clinical cases of COVID-19.

Tool	When to complete	Comments
Person of interest form	To be completed for all individuals suspected of COVID 19 disease and have a specimen taken	
NMC case notification	To be completed for all cases who meet the case definition for COVID-19	Can be completed online using NICD NMC mobile or web based app
Admission form (For inpatients)	To be completed for all confirmed patients admitted to a health care facility at admission or as soon as possible after admission	This form will document presence of co-morbidities, severity of illness at admission
Daily monitoring form (separate forms for inpatients and outpatients)	To be completed for all confirmed patients for each day until they are considered cured (by PCR criteria).	This form will document the daily symptoms, signs and severity of disease during admission
Discharge form (different forms for inpatients and outpatients)	To be completed for all confirmed patients	This form will document patient outcomes such as death, transfer or discharge.
Homecare form (for outpatients)	To be completed for all confirmed patients admitted with mild disease managed at home.	This form will document presence of co-morbidities, severity of illness at admission

The latest version of these forms are available from www.nicd.ac.za

References

1. Fang L, Karakiulakis G, Roth M. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? Lancet Respir Med. 2020.
2. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. N Engl J Med. 2020.
3. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020.
4. Yu P, Zhu J, Zhang Z, Han Y, Huang L. A familial cluster of infection associated with the 2019 novel coronavirus indicating potential person-to-person transmission during the incubation period. J Infect Dis. 2020.
5. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72314 Cases From the Chinese Center for Disease Control and Prevention. JAMA. 2020.
6. World Health Organization. Clinical management of severe acute respiratory infection when novel coronavirus (nCoV) infection is suspected 2020 [Available from: https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected.
7. Schultz MJ, Dunser MW, Dondorp AM, Adhikari NK, Iyer S, Kwizera A, et al. Current challenges in the management of sepsis in ICUs in resource-poor settings and suggestions for the future. Intensive Care Med. 2017;43(5):612-24.
8. Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. Intensive Care Med. 2017;43(3):304-77.
9. Stockman LJ, Bellamy R, Garner P. SARS: systematic review of treatment effects. PLoS Med. 2006;3(9):e343.
10. Lansbury L, Rodrigo C, Leonardi-Bee J, Nguyen-Van-Tam J, Lim WS. Corticosteroids as adjunctive therapy in the treatment of influenza. Cochrane Database Syst Rev. 2019;2:CD010406.
11. Delaney JW, Pinto R, Long J, Lamontagne F, Adhikari NK, Kumar A, et al. The influence of corticosteroid treatment on the outcome of influenza A(H1N1pdm09)-related critical illness. Crit Care. 2016;20:75.
12. Arabi YM, Mandourah Y, Al-Hameed F, Sindi AA, Almekhlafi GA, Hussein MA, et al. Corticosteroid Therapy for Critically Ill Patients with Middle East Respiratory Syndrome. Am J Respir Crit Care Med. 2018;197(6):757-67.
13. Cao B, Wang Y, Wen D, Liu W, Wang J, Fan G, et al. A Trial of Lopinavir–Ritonavir in Adults Hospitalized with Severe Covid-19. New England Journal of Medicine. 2020.
14. Lee MK, Choi J, Park B, Kim B, Lee SJ, Kim SH, et al. High flow nasal cannulae oxygen therapy in acute-moderate hypercapnic respiratory failure. Clin Respir J. 2018;12(6):2046-56.
15. Leung CCH, Joynt GM, Gomersall CD, Wong WT, Lee A, Ling L, et al. Comparison of high-flow nasal cannula versus oxygen face mask for environmental bacterial contamination in critically ill pneumonia patients: a randomized controlled crossover trial. J Hosp Infect. 2019;101(1):84-7.
16. Hui DS, Chow BK, Lo T, Tsang OTY, Ko FW, Ng SS, et al. Exhaled air dispersion during high-flow nasal cannula therapy versus CPAP via different masks. Eur Respir J. 2019;53(4).
17. Hui DS, Chow BK, Lo T, Ng SS, Ko FW, Gin T, et al. Exhaled air dispersion during noninvasive ventilation via helmets and a total facemask. Chest. 2015;147(5):1336-43.
18. Fan E, Del Sorbo L, Goligher EC, Hodgson CL, Munshi L, Walkey AJ, et al. An Official American Thoracic Society/European Society of Intensive Care Medicine/Society of Critical Care Medicine Clinical

Practice Guideline: Mechanical Ventilation in Adult Patients with Acute Respiratory Distress Syndrome. Am J Respir Crit Care Med. 2017;195(9):1253-63.
19. National Heart L, Blood Institute PCTN, Moss M, Huang DT, Brower RG, Ferguson ND, et al. Early Neuromuscular Blockade in the Acute Respiratory Distress Syndrome. N Engl J Med. 2019;380(21):1997-2008.
20. Combes A, Hajage D, Capellier G, Demoule A, Lavoue S, Guervilly C, et al. Extracorporeal Membrane Oxygenation for Severe Acute Respiratory Distress Syndrome. N Engl J Med. 2018;378(21):1965-75.
21. Goligher EC, Tomlinson G, Hajage D, Wijeysundera DN, Fan E, Juni P, et al. Extracorporeal Membrane Oxygenation for Severe Acute Respiratory Distress Syndrome and Posterior Probability of Mortality Benefit in a Post Hoc Bayesian Analysis of a Randomized Clinical Trial. JAMA. 2018;320(21):2251-9.
22. Alshahrani MS, Sindi A, Alshamsi F, Al-Omari A, El Tahan M, Alahmadi B, et al. Extracorporeal membrane oxygenation for severe Middle East respiratory syndrome coronavirus. Ann Intensive Care. 2018;8(1):3.
23. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020.
24. Woelfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, Mueller MA, et al. Clinical presentation and virological assessment of hospitalized cases of coronavirus disease 2019 in a travel-associated transmission cluster. medRxiv. 2020:2020.03.05.20030502.

Appendix 1 – Example of a patient information sheet

Example of a patient information sheet for use with suspected cases who are being sent home to await test results for SARS-CoV-2 (COVID-19).

While awaiting test results for COVID-19 (the novel coronavirus), you have been assessed as being medically well enough to be managed at home.

However, please consider yourself as potentially infectious until the final results are available. You will need to abide by the following:

- You should quarantine yourself at home. Don't go to work, avoid unnecessary travel, and as far as possible avoid close interactions with other people.
- You should clean your hands with soap and water frequently. Alcohol-based sanitizers may also be used, provided they contain at least 60% alcohol.
- Do not have visitors in your home. Only those who live in your home should be allowed to stay. If it is urgent to speak to someone who is not a member of your household, do this over the phone.
- You should wear a facemask when in the same room (or vehicle) as other people.
- At home, you should stay in a specific room and use your own bathroom (if possible). If you live in shared accommodation (university halls of residence or similar) with a communal kitchen, bathroom(s) and living area, you should stay in your room with the door closed, only coming out when necessary, wearing a facemask if one has been issued to you.
- You should practice good cough and sneeze hygiene by coughing or sneezing into a tissue, discarding the tissue immediately afterwards in a lined trash can, and then wash your hands immediately.
- If you need to wash the laundry at home before the results are available, then wash all laundry at the highest temperature compatible for the fabric using laundry detergent. This should be above 60° C. If possible, tumble dry and iron using the highest setting compatible with the fabric. Wear disposable gloves and a plastic apron when handling soiled materials if possible and clean all surfaces and the area around the washing machine. Do not take laundry to a laundrette. Wash your hands thoroughly with soap and water after handling dirty laundry (remove gloves first if used).
- You should avoid sharing household items like dishes, cups, eating utensils and towels. After using any of these, the items should be thoroughly washed with soap and water.
- All high-touch surfaces like table tops, counters, toilets, phones, computers, etc. that you may have touched should be appropriately and frequently cleaned.
- Monitor your symptoms - Seek prompt medical attention if your illness is worsening, for example, if you have difficulty breathing, or if the person you are caring for symptoms are worsening. If it's not an emergency, call your doctor or healthcare facility at the number below. If it is an emergency and you need to call an ambulance, inform the call handler or operator that you are being tested for SARS-CoV-2.

While awaiting the results, if your symptoms worsen:

- Call:

- Or come to:

For more information on COVID-19, see the NICD's FAQ page:

http://www.nicd.ac.za/diseases-a-z-index/covid-19/frequently-asked-questions/

Standard precautions to prevent transmission of COVID-19

Keep your hands clean

When?
- After visiting the bathroom
- Before and after eating
- After blowing your nose
- Whenever you think your hands are dirty

How? Use alcohol hand rub or wash hands with soap and water

Caution Never touch your eyes, nose or mouth with unwashed hands

Cough etiquette
- Keep a distance of 2 meters between you and a person with a cough
- Cover your own cough or sneeze with a tissue
- Once used, throw the tissue away in a closed container
- Clean your hands afterwards

- **Do not share items with other people** (clothing, blankets, pillows, towels, mobile phones, uncovered food, magazines, books)
- **Do not keep the toilet lid up when you flush the toilet** (you can transmit the virus from all body excretions)

Keep your immediate environment clean
- Wipe frequently-touched areas regularly with a disinfectant cloth
- Discard all waste immediately