

INTERIM COVID-19 CLINICAL MANAGEMENT GUIDELINES

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COVID-19 CLINICAL MANAGEMENT COMMITTEE (CCMC)

MINISTRY OF HEALTH





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SITING OF CARE FOR COVID-19 PATIENTS

Summary: Siting of care for COVID-19 patients

	All Covid-19 infected patients need to be triaged by severity of disease. After triage, all Covid-19 infected patients are to be prioritised for admission based on the assessed risk of deterioration and developing complications. The assessment includes time point of infection, clinical parameters, and risk factors including age, clinical comorbidities, and BMI.
	Patients who have mild disease and low risk of complications should be monitored for clinical deterioration using parameters such as temperature, pulse rate and oxygen saturation.
	Routine imaging of the chest is not needed for all patients especially those with mild disease. It is indicated for patients with abnormal vital signs or clinical signs of pneumonia.
	Patients with moderate or severe disease should be closely monitored in the hospital setting and risks of deterioration should be assessed using chest radiography, laboratory markers such as C-reactive protein, or clinical risk scores

Note: the classification of COVID-19 clinical severity and the description for each grade of severity can be found on page 8

COVID-19 Clinical Management Recommendations on Siting of Care

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
1	All Covid-19 infected patients need to be triaged by severity of disease. After triage, all Covid-19 infected patients are to be prioritised for admission based on the assessed risk of deterioration and developing complications. The assessment includes time point of infection, clinical parameters, and risk factors including age, clinical comorbidities, and BMI.	IV	C	Moderate	Y
2	Patients who have mild disease and low risk of complication should be monitored for clinical deterioration using parameters such as temperature, pulse rate and oxygen saturation.	V	D	Weak	Y
3	Routine imaging of the chest is not needed for all patients especially those with mild disease. It is indicated for patients with abnormal vital signs or clinical signs of pneumonia.	IV	C	Moderate	Y
4	Patients with moderate or severe disease should be closely monitored in the hospital setting	IV	C	Moderate	Y

	and risks of deterioration should be assessed using chest radiography, laboratory markers such as C-reactive protein, or clinical risk scores.				
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For further details on the acute COVID-19 care recommendations, please also refer to the *Treatment Guidelines for COVID-19* developed by the National Centre for Infectious Diseases and the Chapter of Infectious Disease Physicians (<https://www.ncid.sg/Health-Professionals/Diseases-and-Conditions/Pages/COVID-19.aspx>)

Discussion

Recommendations 1 & 2:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
1	All Covid-19 infected patients need to be triaged by severity of disease. After triage, all Covid-19 infected patients are to be prioritised for admission based on the assessed risk of deterioration and developing complications. The assessment includes time point of infection, clinical parameters, and risk factors including age, clinical comorbidities, and BMI.	IV	C	Moderate	Y
2	Patients who have mild disease and low risk of complication should be monitored for clinical deterioration using parameters such as temperature, pulse rate and oxygen saturation.	V	D	Weak	Y

In our local experience, the majority of COVID-19 cases are subclinical. Many of them are asymptomatic and are detected on routine testing. The risks of developing clinical complications are highest in patients with persistent symptoms extending into the second week of infection and directly related to patient's age and clinical comorbidities including diabetes mellitus, hypertension, high BMI or chronic organ diseases. The risk of patients requiring oxygen support or ICU admission increases to more than 10% for patients more than 45 years old or in those with abnormal CXR.

The clinical severity of COVID-19 can be classified as below and is used to describe disease severity in this document*:

COVID-19 severity	
Asymptomatic or Presymptomatic	Test positive for SARS-CoV-2 with a virologic test but have no symptoms consistent with COVID-19
Mild	Any signs/symptoms of COVID-19 (e.g. fever, cough, sore throat, malaise, headache, myalgia, nausea, vomiting, diarrhoea, loss of taste/smell) but who do not have shortness of breath or clinical signs of pneumonia or abnormal chest imaging
Moderate	Shows evidence of lower respiratory tract disease during clinical assessment or imaging, and have an SpO2 of $\geq 94\%$ on room air.
Severe	Individuals who have a SpO2 of $<94\%$ on room air, or P/F ratio of <300 mmHg, respiratory rate of >30 breaths/minute or lung infiltrates occupying $>50\%$ of lung fields
Critical	Individuals with respiratory failure, septic shock, and/or multiple organ dysfunction

*COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Available at <https://www.covid19treatmentguidelines.nih.gov/>. Accessed 15 Dec 2020.

Recommendation 3:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
3	Routine imaging of the chest is not needed for all patients especially those with mild disease. It is indicated for patients with abnormal vital signs or clinical signs of pneumonia.	IV	C	Moderate	Y

Both international consensus and local experience show that chest imaging is not indicated routinely in mild asymptomatic patients who are well. CXR is indicated to assess for pneumonia in patients who are suspected to have pneumonia or who are at risk of developing pulmonary complications. Chest imaging should be repeated if there is deterioration in the pulmonary status. Pneumonia may develop/worsen in a subgroup of COVID-19 patients around days 6-10 of symptomatic illness.

Chest X-ray indications for persons with COVID-19 at Community Care Facilities:

1. At least one of the following abnormal vital signs:
 - a. Temperature >37.8°C
 - b. Persistent heart rate > 100 beats/minute
 - c. Persistent respiratory rate > 20 breaths/minute
 - d. Persistent SpO₂ <94% (at rest) or desaturation to below 94% on 6 minute-walk-test

AND/OR

2. At least two of the following clinical findings
 - a. Decreased breath sounds/bronchial breath sounds
 - b. Crepitation or wheezes
 - c. Absence of asthma

AND/OR

3. Abnormal POCUS (Point of care ultrasound) lung (done by credentialed operator)

**Endorsed by the Community Care Facility Medical Board and MOH Public Health and Clinical Workgroup, 30 Sep 2020.

Recommendation 4:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
4	Patients with moderate or severe disease should be closely monitored in the hospital setting and risks of deterioration should be assessed using chest radiography, laboratory markers such as C-reactive protein, or clinical risk scores.	IV	C	Moderate	Y

A variety of risk scores have been validated in our local setting and these include a combination of clinical risk factors, white blood cell indices (neutrophil count, lymphocyte count and neutrophil-lymphocyte ratio), biochemical parameters (CRP, LDH). The *Rule-of-6* score using a first 48-hour assessment of ferritin >600 ug/l, LDH >600U/L and CRP >60 mg/L will predict for patients at risk of deterioration². For simplicity, if only CRP is used as a prognosticator, a cut-off of > 20 mg/L was found the best balance of sensitivity and specificity for predicting severe/critical illness³, and was comparable to other published and more complicated clinical risk scores (see table below). An abnormal CXR between Day 6-10 of disease onset also performed equally well for predicting disease progression⁴.

	AUC in this cohort (95% CI)	Youden's Index (95% CI)	Cut-off Value	Sensitivity	Specificity
CRP (n-694)	0.90 (0.87-0.92)	0.65 (0.52-0.71)	>21.5	78%	88%









Data courtesy of Dr Barnaby Young (NCID)

References

1. National Centre for Infectious Diseases, Chapter of Infectious Disease Physicians College of Physicians Singapore. (2021). *Interim Treatment Guidelines for COVID-19*. Accessed from <https://www.ncid.sg/Health-Professionals/Diseases-and-Conditions/Pages/COVID-19.aspx> on February 16, 2021.
2. Lee Dickens et al. Simple “Rule-of-6” predicts severe Coronavirus Disease 2019 (COVID-19) *Clinical Infectious Disease* 2020, <https://doi.org/10.1093/cid/ciaa938>
3. Young B (Unpublished data), National Centre for Infectious Diseases
4. Hui TCH. Clinical utility of chest radiography for severe COVID-19. *Quant Imaging Med Surg.* 2020; 10:1540-1550.

**RECOMMENDATIONS FOR COVID-19 PATIENTS REQUIRING
INTENSIVE CARE**

Summary: Clinical Management of Critically Ill COVID-19 Patients

	Patients should be admitted to ICU based on the severity of their clinical condition and resource availability. Each hospital should determine early referral criteria for evaluation by the ICU team.
	The critical care management of patients with COVID-19 should not differ substantially from the management of other critically ill patients. Attention should be paid to the primary process leading to the ICU admission, but also to underlying comorbidities and nosocomial complications.
Ventilatory Support	
	For adults with COVID-19 and acute hypoxemic respiratory failure despite conventional oxygen therapy, we recommend high-flow nasal cannula (HFNC) oxygen over non-invasive positive pressure ventilation (NIPPV).
	In the absence of an indication for endotracheal intubation, we recommend a closely monitored trial of NIPPV for adults with COVID-19 and acute hypoxemic respiratory failure for whom HFNC is not available.
	For adults with COVID-19 who are receiving supplemental oxygen, we recommend close monitoring for worsening respiratory status and that intubation, if it becomes necessary, be performed by an experienced practitioner in a controlled setting.
	For patients with persistent hypoxemia despite increasing supplemental oxygen requirements in whom endotracheal intubation is not otherwise indicated, we recommend considering a trial of awake prone positioning to improve oxygenation.
	For mechanically ventilated adults with COVID-19 and acute respiratory distress syndrome (ARDS), we recommend using low tidal volume (VT) ventilation (VT 4–8 mL/kg of predicted body weight) over higher tidal volumes (VT >8 mL/kg).
	For mechanically ventilated adults with COVID-19 and refractory hypoxemia despite optimized ventilation, we recommend prone ventilation for 12 to 16 hours per day over no prone ventilation.

COVID-19 Clinical Management Recommendations of Critically Ill COVID-19 Patients

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
1	Patients should be admitted to ICU based on the severity of their clinical condition and resource availability. Each hospital should determine early referral criteria for evaluation by the ICU team.	IV	C	Moderate	Y
2	The critical care management of patients with COVID-19 should not differ substantially from the management of other critically ill patients. Attention should be paid to the primary process leading to the ICU admission, but also to underlying comorbidities and nosocomial complications.	V / Ungraded	D	Weak Good Practice	N
3	For adults with COVID-19 and acute hypoxemic respiratory failure despite conventional oxygen therapy, we recommend high-flow nasal cannula (HFNC) oxygen over non-invasive positive pressure ventilation (NIPPV).	V / Ungraded	D	Weak Good Practice	N
4	In the absence of an indication for endotracheal intubation, we recommend a closely monitored trial of NIPPV for adults with COVID-19 and acute hypoxemic respiratory failure for whom HFNC is not available.	V / Ungraded	D	Weak Good Practice	N

5	For adults with COVID-19 who are receiving supplemental oxygen, we recommend close monitoring for worsening respiratory status and that intubation, if it becomes necessary, be performed by an experienced practitioner in a controlled setting.	V / Ungraded	D	Weak Good Practice	N
6	For patients with persistent hypoxemia despite increasing supplemental oxygen requirements in whom endotracheal intubation is not otherwise indicated, we recommend considering a trial of awake prone positioning to improve oxygenation.	II	B	Moderate	Y
7	For mechanically ventilated adults with COVID-19 and acute respiratory distress syndrome (ARDS), we recommend using low tidal volume (VT) ventilation (VT 4–8 mL/kg of predicted body weight) over higher tidal volumes (VT >8 mL/kg).	I	A	Strong	N
8	For mechanically ventilated adults with COVID-19 and refractory hypoxemia despite optimized ventilation, we recommend prone ventilation for 12 to 16 hours per day over no prone ventilation.	II	B	Strong	N

Discussion

Recommendation 1:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
1	Patients should be admitted to ICU based on the severity of their clinical condition and resource availability. Each hospital should determine early referral criteria for evaluation by the ICU team.	IV	C	Moderate	Y

We recommend that patients should be admitted to ICU based on the severity of their clinical condition and resource availability. During outbreaks, a surge of patients may exhaust resources; less severe cases may need to be managed outside the ICU.

Each hospital should determine early referral criteria for evaluation by the ICU team. A severely ill patient should be transferred early to ICU for closer monitoring so that intubation, when indicated, can be performed in a controlled setting.

Suggested referral criteria¹:

1. Respiratory Rate \geq 30/min or progressive respiratory failure
2. FiO₂ requirement > 50% face mask
3. Hypotension requiring vasopressors (or lack of response to fluid resuscitation)

Recommendation 2:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
2	The critical care management of patients with COVID-19 should not differ substantially from the management of other critically ill patients. Attention should be paid to the primary process leading to the ICU admission, but also to underlying comorbidities and nosocomial complications.	V / Ungraded	D	Weak Good Practice	N

We recommend that the critical care management of patients with COVID-19 should not differ substantially from the management of other critically ill patients. As with any patient in the ICU, successful clinical management of a patient with COVID-19 depends on attention to the primary process leading to the ICU admission, but also to underlying comorbidities and nosocomial complications. Severe cases of COVID-19 may be associated with acute respiratory distress syndrome, septic shock, cardiac dysfunction, elevations in multiple inflammatory cytokines, thromboembolic disease, renal function impairment and/or exacerbation of underlying comorbidities.

Because critically ill patients with COVID-19 are likely to undergo aerosol-generating procedures, we recommend that they should be placed in airborne infection isolation rooms, when available. Health care workers should be in appropriate personal protective gear as per prevailing guidelines.

Recommendations 3-8:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
3	For adults with COVID-19 and acute hypoxemic respiratory failure despite conventional oxygen therapy, we recommend high-flow nasal cannula (HFNC) oxygen over non-invasive positive pressure ventilation (NIPPV).	V / Ungraded	D	Weak Good Practice	N
4	In the absence of an indication for endotracheal intubation, we recommend a closely monitored trial of NIPPV for adults with COVID-19 and acute hypoxemic respiratory failure for whom HFNC is not available.	V / Ungraded	D	Weak Good Practice	N
5	For adults with COVID-19 who are receiving supplemental oxygen, we recommend close monitoring for worsening respiratory status and that intubation, if it becomes necessary, be performed by an experienced practitioner in a controlled setting.	V / Ungraded	D	Weak Good Practice	N

6	For patients with persistent hypoxemia despite increasing supplemental oxygen requirements in whom endotracheal intubation is not otherwise indicated, we recommend considering a trial of awake prone positioning to improve oxygenation.	II	B	Moderate	Y
7	For mechanically ventilated adults with COVID-19 and acute respiratory distress syndrome (ARDS), we recommend using low tidal volume (VT) ventilation (VT 4–8 mL/kg of predicted body weight) over higher tidal volumes (VT >8 mL/kg).	I	A	Strong	N
8	For mechanically ventilated adults with COVID-19 and refractory hypoxemia despite optimized ventilation, we recommend prone ventilation for 12 to 16 hours per day over no prone ventilation.	II	B	Strong	N

Recommendations 3 to 8 give guidance on ventilatory support of critically ill COVID-19 patients. As an additional note, there is insufficient data to recommend either for or against the routine use of extracorporeal membrane oxygenation (ECMO) for patients with COVID-19 and refractory hypoxemia.

The eligibility criteria for adult ECMO (in accordance with recommendations from the National Extracorporeal Membrane Oxygenation (ECMO) Services Advisory Workgroup) are:










- 1 Decisions on ECMO initiation are made on a case-by-case basis with regards to the risks and benefits. If the referring physician considers the patient to be an ECMO candidate, he/she should discuss it with the ECMO centre.
- 2 Triggers for ECMO activation should take into account the patient's trajectory of illness e.g. rate of deterioration and the COVID-19 outbreak situation.
- 3 Indications for veno-venous ECMO (VV-ECMO) in acute respiratory failure. ECMO should be reserved for patients who are at a high risk of death despite maximal conventional therapy, including those with:
 - a. Severe hypoxaemia e.g. $\text{PaO}_2/\text{FiO}_2 < 80$ on $\text{FiO}_2 > 90\%$, despite optimal positive end-expiratory pressure (PEEP), oxygen and adjunct therapies e.g. paralysis, prone positioning
 - b. Severe hypercapnic respiratory acidosis ($\text{pH} < 7.15$)
 - c. Inability to achieve lung protective ventilation e.g. tidal volume ≤ 6 mls/kg, plateau pressure ≤ 30 cm H₂O
 - d. Significant air leak/barotrauma
- 4 General contraindications for VV-ECMO in acute respiratory failure:
 - a. Age > 70 years
 - b. Presence of advanced multi-organ failure
 - c. Severe chronic organ failure e.g. kidney, liver, lung
 - d. Advanced malignancy
 - e. Severe brain injury
 - f. Pre-existing "do not resuscitate" order
 - g. Uncontrolled bleeding
 - h. Immediately following cardiac arrest
 - i. Patients with chronic immunosuppression
 - j. Invasive mechanical ventilation for ≥ 7 days prior

References

1. Tai DY. SARS: how to manage future outbreaks? *Ann Acad Med Singap.* 2006 May;35(5):368-73. PMID: 16830006.
2. COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Available at <https://www.covid19treatmentguidelines.nih.gov/>. Accessed 4 Nov 2020.
3. World Health Organization (2020). Clinical Care for Severe Acute Respiratory Infection Toolkit. ; 2020 (WHO/2019- nCoV/SARI_toolkit/2020.1). Licence: CC BY-NC-SA 3.0 IGO.

HAEMATOLOGY RECOMMENDATIONS FOR COVID-19 PATIENTS

Summary: Anticoagulation in COVID-19 patients

	We recommend that thromboembolic risk assessment, e.g. the PADUA score, be done as part of the admission process for COVID-19 patients at out-of-hospital facilities. Persons at high risk of venous thromboembolism (VTE) should be assessed for thromboprophylaxis with an appropriate agent and duration at an acute hospital.
	All COVID-19 patients should have thrombotic and bleeding risk assessments such as the PADUA score and the VTE bleed score upon diagnosis.
	In patients with mild/moderate COVID-19 infection, we recommend risk stratification of patients, such as with the PADUA risk score, to determine whether pharmacological thromboprophylaxis is warranted.
	In patients with severe COVID-19 infection, we recommend pharmacological thromboprophylaxis unless contraindicated.
	Patients should be educated on general measures to prevent thromboembolism or seek urgent consultation for symptoms of thromboembolism.
	Patients should be encouraged to maintain hydration and to avoid immobility, to reduce the risk of thromboembolism.
	D-dimer should not be used as a screening tool for VTE. It should be used as a diagnostic tool of exclusion
	Therapeutic anticoagulation doses, or doses higher than for prophylaxis, should not be used without confirmation of thrombosis.
	Routine antiplatelet prophylaxis for all COVID recovered patients are not recommended at this point.

COVID-19 Clinical Management Recommendations by Haematology

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
1	We recommend that thromboembolic risk assessment, e.g. the PADUA score, be done as part of the admission process for COVID-19 patients at out-of-hospital facilities. Persons at high risk of venous thromboembolism (VTE) should be assessed for thromboprophylaxis with an appropriate agent and duration at an acute hospital.	V	D	Weak	N
2	All COVID-19 patients should have thrombotic and bleeding risk assessments such as the PADUA score and the VTE bleed score upon diagnosis.	V	D	Weak	N
3	In patients with mild/moderate COVID-19 infection, we recommend risk stratification of patients, such as with the PADUA risk score, to determine whether pharmacological thromboprophylaxis is warranted.	V	D	Weak	N
4	In patients with severe COVID-19 infection, we recommend pharmacological thromboprophylaxis unless contraindicated.	V	D	Weak	N
5	Patients should be educated on general	V	D	Weak	N

	measures to prevent thromboembolism or seek urgent consultation for symptoms of thromboembolism.				
6	Patients should be encouraged to maintain hydration and to avoid immobility, to reduce the risk of thromboembolism.	V	D	Weak	N

Discussion

Recommendations 1 & 2:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
1	We recommend that thromboembolic risk assessment, e.g. the PADUA score, be done as part of the admission process for COVID-19 patients at out-of-hospital facilities. Persons at high risk of venous thromboembolism (VTE) should be assessed for thromboprophylaxis with an appropriate agent and duration at an acute hospital.	V	D	Weak	N
2	All COVID-19 patients should have thrombotic and bleeding risk assessments such as PADUA score and VTE bleed score upon diagnosis.	V	D	Weak	N

We recommend that persons in this category with high risk of VTE (PADUA score ≥ 4 points) be administered thromboprophylaxis of SC enoxaparin 40mg once daily or renal adjusted dose of 20mg once daily, until discharge from the out-of-hospital facility.

Recommendation 3:

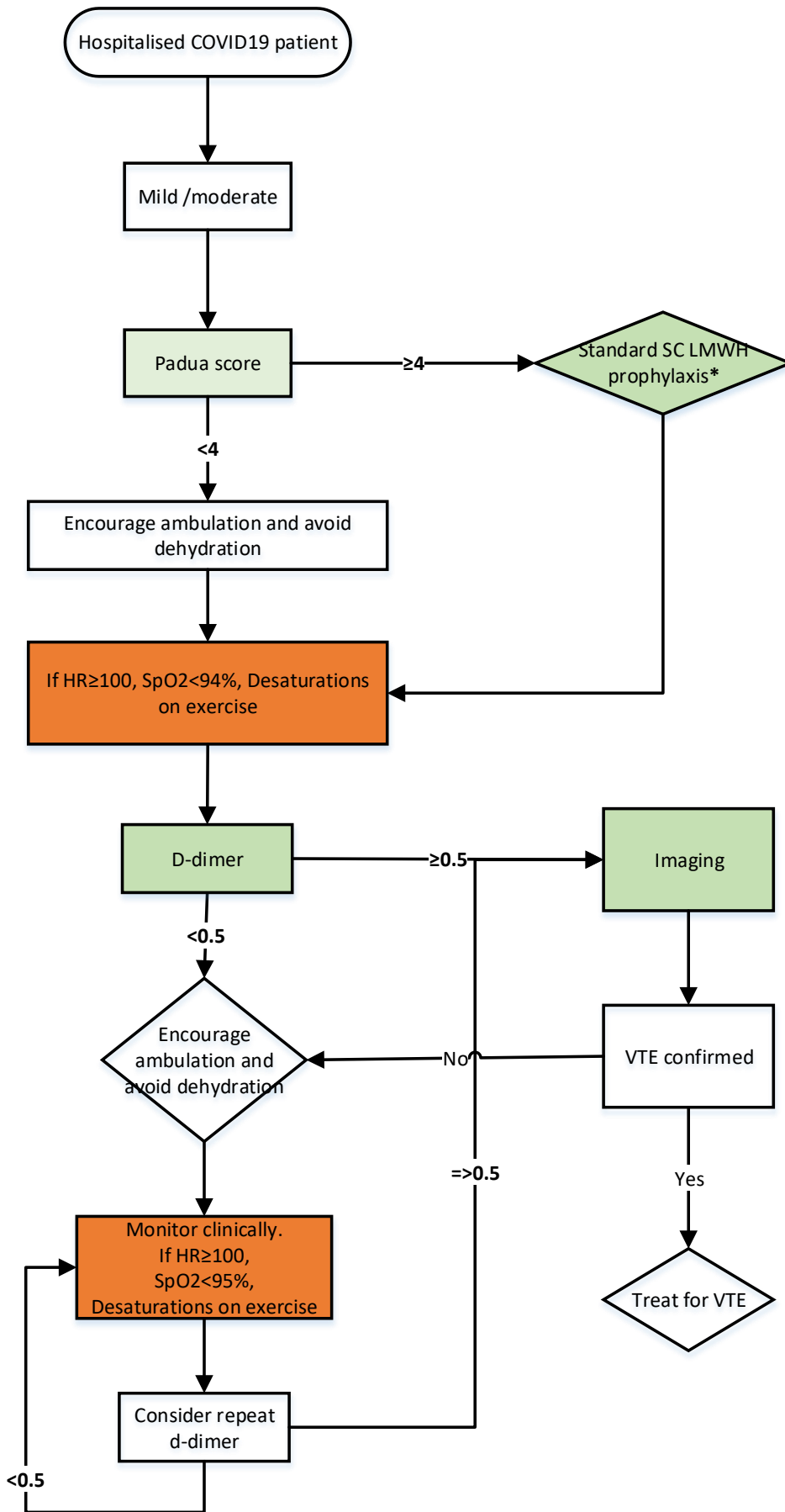
SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
3	In patients with mild/moderate COVID-19 infection, we recommend risk stratification of patients, such as with the PADUA risk score, to determine whether pharmacological thromboprophylaxis is warranted.	V	D	Weak	N

Proposed Guide for Thromboprophylaxis Decision Making in Patients with Mild/Moderate COVID-19

PADUA Score (≥4 points = high VTE risk)	
Risk factor	Points
Active cancer	3
Previous VTE	3
Reduced mobility	3
Known thrombophilia	3
Recent (<1 month) surgery	4
Elderly (age >70)	1
Heart or respiratory failure	1
Acute MI or stroke	1
Acute infection and/or rheumatologic disorder	1
Obesity (BMI >30)	1
Ongoing hormonal treatment	1

Notes:

1. In the absence of a locally validated scoring system, we propose to adopt PADUA risk stratification, acknowledging that it has not been extensively validated in the Asian/Singaporean population.
2. COVID-19 is not an additional risk factor in PADUA score – it should be scored as an acute infection and be assigned a score of 1.
3. D-dimer is a diagnostic tool of exclusion, and not to be used for screening.
4. Risk of thromboembolism must be weighed against the risk of bleeding (use of VTE-Bleed score)
5. We recommend against escalation of anticoagulant dosing based only on biomarkers, such as D-dimer. However, acutely worsening clinical status in conjunction with laboratory value changes, such as rising D-dimer, may necessitate further thromboembolic workup or empiric treatment.
6. For lower limb DVT or PE **provoked** by COVID-19, the recommended length of treatment is **3 months**



SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
4	In patients with severe COVID-19 infection, we recommend pharmacological thromboprophylaxis unless contraindicated.	V	D	Weak	N

For this purpose, patients with severe COVID-19 includes patients:

- a. Requiring ICU admission
- b. Requiring high dependency / ICA admission
- c. In general ward requiring oxygen supplementation

In these patients, we recommend pharmacological thromboprophylaxis with the standard prophylactic dose of low molecular weight heparin (LMWH) or unfractionated heparin. These include:

- a. LMWH: SC enoxaparin 40mg once daily or renal adjusted dose of 20mg once daily
- b. Unfractionated heparin: SC heparin 5000IU twice daily

We **do not** recommend higher than prophylaxis doses.

In this group of patients with contraindications to pharmacological thromboprophylaxis, we recommend the use of pneumatic calf pumps.

We recommend that treating clinicians have a high index of suspicion and low threshold for imaging in situations where VTEs are suspected.

Recommendations 5 & 6:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
5	Patients should be educated on general measures to prevent thromboembolism or seek urgent consultation for symptoms of thromboembolism.	V	D	Weak	N
6	Patients should be encouraged to maintain hydration and to avoid immobility, to reduce the risk of thromboembolism	V	D	Weak	N




COVID-19 may be associated with increased risks of thromboembolism, which may be exacerbated by isolation measures. Thromboembolism may be prevented by maintaining hydration and avoiding immobility. Patients should also be educated on features of thromboembolism so that they may recognise the need to seek early medical attention.

References




1. Chuen Wen Tan, MB BCh BAO, FRCPath^{1*}; Jing Yuan Tan, MBBS^{2*}; Wan Hui Wong, PhD¹; May Anne Cheong, MRCP¹; Ian Matthias Ng, MBBS³; Edwin Philip Conceicao, BSc³; Jenny Guek Hong Low, MBBS, MPH^{4,5}; Heng Joo Ng, MBBS, FRCPath¹; Lai Heng Lee, MBBS¹. Clinical and laboratory features of hypercoagulability in COVID-19 and other respiratory viral infections amongst predominantly younger adults with few comorbidities. Scientific Reports (in press)

CARDIOLOGY RECOMMENDATIONS FOR COVID-19 PATIENTS

Summary: Aspirin use in active or recovered COVID-19 patients with coronary artery disease (CAD)

	In patients with known CAD, and not on any other anti-thrombotic or anti-coagulant for other reasons, aspirin use should be continued as secondary prevention.
	Aspirin may be considered in individuals aged 40-70 with high ASCVD risk but not at increased risk of bleeding.
	Routine aspirin use in active or recovered COVID-19 patients without known CAD is not recommended because there is insufficient data to demonstrate clinical benefit AND because aspirin use is not without risk.

Summary: Evaluation of chest pain and dyspnoea in recovered COVID-19 patients in primary care setting

	COVID-19 has been associated with increased incidence of acute coronary syndrome, myocarditis, arrhythmias and pulmonary embolism. Active or recovered COVID-19 patients with cardiovascular symptoms of chest pain, dyspnoea and palpitations should be evaluated, even in the absence of typical cardiovascular risk factors.
	Use of the Well's score and CAD consortium risk score should be part of the risk assessment for COVID-19 patients presenting with chest pain or dyspnoea.
	ECG, troponins, BNP (or NT-pro-BNP), D-dimer and CXR should be considered as part of the workup.

COVID-19 Clinical Management Recommendations by Cardiology

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
1	In patients with known CAD, and not on any other anti-thrombotic or anti-coagulant for other reasons, aspirin use should be continued as secondary prevention.	V	D	Weak	N
2	Aspirin may be considered in individuals aged 40-70 with high ASCVD risk but not at increased risk of bleeding.	V	D	Weak	N
3	COVID-19 has been associated with increased incidence of acute coronary syndrome, myocarditis, arrhythmias and pulmonary embolism. Active or recovered COVID-19 patients with cardiovascular symptoms of chest pain, dyspnoea and palpitations should be evaluated, even in the absence of typical cardiovascular risk factors.	IV	C	Moderate	N
4	Use of the Well's score and CAD consortium risk score should be part of the risk assessment for COVID-19 patients presenting with chest pain or dyspnoea.	V	D	Weak	N
5	ECG, troponins, BNP (or NT-pro-BNP), D-dimer and CXR should be considered as part of the workup.	IV	C	Moderate	N

Discussion

Recommendation 1:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
1	In patients with known CAD, and not on any other anti-thrombotic or anti-coagulant for other reasons, aspirin use should be continued as secondary prevention.	V	D	Weak	N

In patients with known coronary artery disease (CAD), and not on any other anti-thrombotic or anticoagulant for other reasons, life-long aspirin use is indicated as secondary prevention given that there is already underlying CAD. There is extensive evidence from studies of non-COVID-19 patients, and it is widely recommended for the secondary prevention of atherosclerotic cardiovascular disease (ASCVD) including CAD^{41,42,43}. However, while there is a paucity of data relating to COVID-19, with emerging evidence that COVID-19 predisposes to a prothrombotic state, it is reasonable to continue to treat these patients with aspirin as secondary prevention of ASCVD if there are no contraindications.

Recommendation 2:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
2	Aspirin may be considered in individuals aged 40-70 with high ASCVD risk but not at increased risk of bleeding.	V	D	Weak	N

While aspirin use for primary prevention of CAD has been practiced widely for many years, more recent studies and meta-analyses have shown the benefits to be heterogeneous and modest⁴⁴. As such, aspirin use for primary prevention of CAD is not recommended for most patients. Some guidelines do recommend it for individuals at high risk of ASCVD but to avoid it in patients with higher bleeding risk, including older patients^{33,45}. We hence recommend that it may be considered in individuals aged 40-70 with high ASCVD risk but not at increased risk of bleeding³³.

It should be noted that there is no evidence for the routine aspirin use in COVID-19/recovered COVID-19 persons without known CAD. Moreover, aspirin use has been associated with risks of bleeding complications and gastritis, and as such, we do not recommend its routine use in such patients.

Recommendation 3:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
3	COVID-19 has been associated with increased incidence of acute coronary syndrome, myocarditis, arrhythmias and pulmonary embolism. Active or recovered COVID-19 patients with cardiovascular symptoms of chest pain, dyspnoea and palpitations should be evaluated, even in the absence of typical cardiovascular risk factors.	IV	C	Moderate	N

COVID-19 has been associated with major adverse cardiovascular events, with both clinical and post-mortem reports of acute coronary syndromes, myocarditis, arrhythmias and pulmonary embolism.^{1,2,3,4,5} The presence of cardiac complications is also independently associated with increased mortality.^{6,7} As such, cardiovascular events should be assessed for when active or recovered COVID-19 patients present with cardiovascular symptoms such as chest pain, dyspnoea and palpitations, even in the absence of typical cardiovascular risk factors.^{1,8,9}

Recommendation 4:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
4	Use of the Well's score and CAD consortium risk score should be part of the risk assessment for COVID-19 patients presenting with chest pain or dyspnoea.	V	D	Weak	N

In the clinical evaluation of COVID-19 patients presenting with chest pain or dyspnoea, using risk scoring methods such as the Well's score¹⁰ and CAD consortium score¹¹ is recommended to aid in deciding the appropriate management for each patient. A proposed workflow for is shown in Figure 2. While the use of Well's score and the CAD consortium score have been shown to be helpful in risk stratification for pulmonary embolism and coronary artery disease, there are no data on the applicability specifically in COVID-19 patients. However, there are case reports, and case series of pulmonary embolism¹²⁻²⁴; as well as limited data on acute coronary syndromes²⁵⁻³¹. For acute myocardial infarctions, local data suggest no significant change in case incidence³².

Recommendation 5:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
5	ECG, troponins, BNP (or NT-pro-BNP), D-dimer and CXR should be considered as part of the workup.	IV	C	Moderate	N

For investigations, an ECG, blood tests such as troponins, BNP (or NT-pro-BNP) and D-dimer, and a CXR are recommended^{1,2,5,6,7,34,35,36}. Levels of quantitative markers of cardiomyocyte stress and injury such as troponin and BNP (or NT-pro-BNP) and makers of coagulopathy such as D-dimer correlate with COVID-19 severity and mortality^{2,6,7,34,35,37,38,39,40}. If the ECG and blood tests are within normal limits and CXR is unremarkable, patient may be discharged for follow-up review as necessary.

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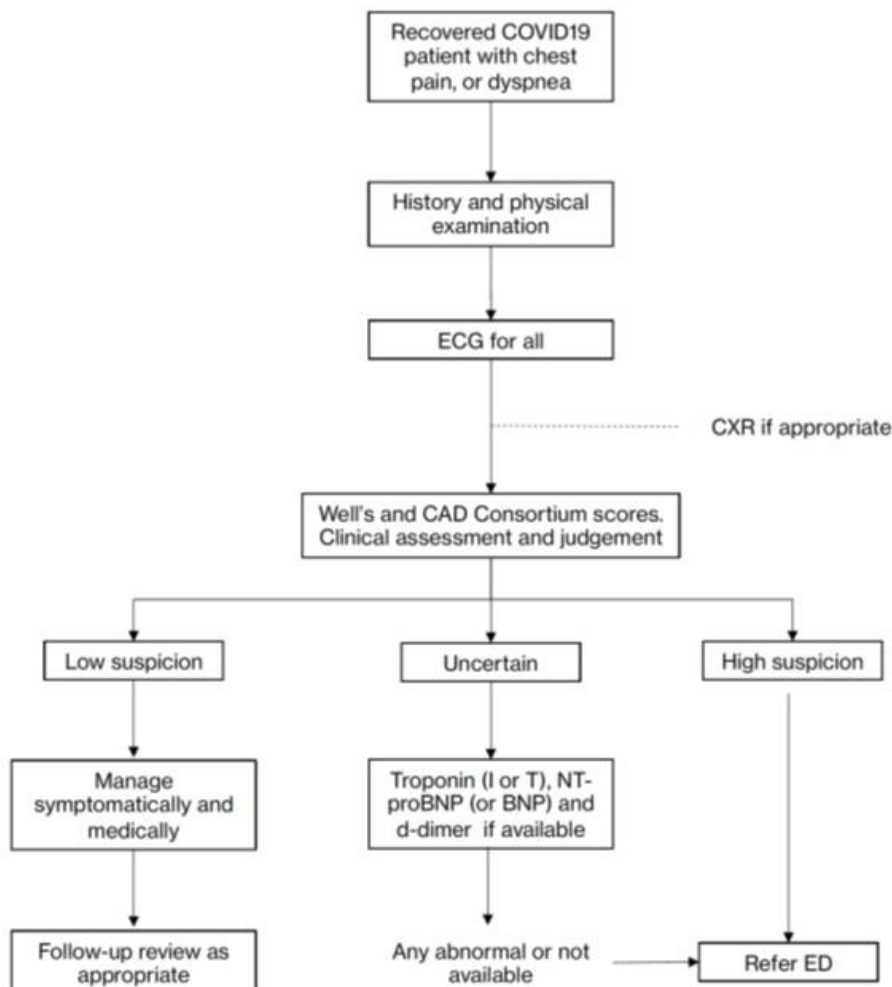
ANNEX

Figure 1: Well's score

Features	Score (points)
Clinical signs and symptoms of DVT	3.0
No alternative diagnosis	3.0
Heart rate >100 beats/min	1.5
Immobilization ≥3 days or surgery in the previous 4 weeks	1.5
Previous DVT or PE	1.5
Hemoptysis	1.0
Malignancy with active treatment in the past 6 months or under palliative care	1.0
Pretest clinical probability	
PE unlikely	≤4.0
PE likely	>4.0






PE = Pulmonary embolism, DVT = Deep vein thrombosis

Figure 2: Proposed workflow for recovered COVID-19 patients presenting to primary care with chest pain or dyspnoea



RESPIRATORY MEDICINE RECOMMENDATIONS FOR COVID-19
PATIENTS

Summary: Clinical Management of Respiratory Issues

	Pulmonary rehabilitation should be considered in COVID-19 patients with chronic obstructive pulmonary disease (COPD), but there is insufficient evidence to recommend it routinely for COVID-19 patients.
	Long term oxygen therapy for chronic hypoxaemia should be considered in patients with COVID 19 and concomitant COPD.
	Recovered patients with abnormal chest X-ray (CXR) findings should be followed up till resolution and a repeat CXR may be required at 7-12 weeks. No further investigations or follow-up is otherwise required in the absence of persisting symptoms or CXR abnormalities.
	Where further evaluation is indicated, computed tomography of the thorax (CT thorax) and a full lung function test may be considered. Lung function tests should be performed only when the patient is no longer infectious.
	Patients with COVID-19 and Acute Respiratory Distress Syndrome (ARDS) will need longer term follow-up with repeat lung function testing and /or radiological imaging at appropriate intervals depending on their clinical status.

COVID-19 Clinical Management Recommendations by Respiratory Medicine

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
1	Pulmonary rehabilitation should be considered in COVID-19 patients with chronic obstructive pulmonary disease (COPD), but there is insufficient evidence to recommend it routinely for COVID-19 patients.	I	A	Strong	N
2	Long term oxygen therapy for chronic hypoxaemia should be considered in patients with COVID 19 and concomitant COPD.	I	A	Strong	N
3	Recovered patients with abnormal chest X-ray (CXR) findings should be followed up till resolution and a repeat CXR may be required at 7-12 weeks. No further investigations or follow-up is otherwise required in the absence of persisting symptoms or CXR abnormalities.	V	D	Weak Good Practice	N
4	Where further evaluation is indicated, computed tomography of the thorax (CT thorax) and a full lung function test may be considered. Lung function tests should be performed only when the patient is no longer infectious.	V	D	Weak Good Practice	N
5	Patients with COVID-19 and Acute Respiratory Distress Syndrome (ARDS) will need longer term follow-up with repeat lung function testing and	V	D	Weak Good Practice	N

	/or radiological imaging at appropriate intervals depending on their clinical status.				
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Discussion

Recommendation 1:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
1	Pulmonary rehabilitation should be considered in COVID-19 patients with chronic obstructive pulmonary disease (COPD), but there is insufficient evidence to recommend it routinely for COVID-19 patients.	I	A	Strong	N

The strongest evidence for pulmonary rehab is seen in COVID-19 patients with chronic obstructive pulmonary disease (COPD) patients.

There is currently not enough evidence to recommend routine pulmonary rehabilitation for COVID-19 patients at this stage though these patients may experience similar symptoms and are functionally limited. Evidence for pulmonary rehabilitation in patients with other chronic respiratory diseases other than COPD is weak and has to be assessed on a case-by-case basis.

Recommendation 2:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
2	Long term oxygen therapy for chronic hypoxaemia should be considered in patients with COVID 19 and concomitant COPD.	I	A	Strong	N

There is strong evidence for use of long-term oxygen therapy for chronic hypoxaemia in patients with COVID 19 and concomitant COPD. For other cardiorespiratory diseases, the evidence for use of long-term oxygen therapy is extrapolated from the benefits derived from COPD.

Recommendation 3:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
3	Recovered patients with abnormal chest X-ray (CXR) findings should be followed up till resolution and a repeat CXR may be required at 7-12 weeks. No further investigations or follow-up is otherwise required in the absence of persisting symptoms or CXR abnormalities.	V	D	Weak Good Practice	N

It is recommended that recovered patients with abnormal Chest X-ray (CXR) findings be followed up till resolution. A repeat CXR may be required at 7-12 weeks.

On the other hand, no further investigations or follow-up is required unless there are persistent CXR changes or if patient remains symptomatic (breathless, cough)

Recommendations 4 & 5:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
4	Where further evaluation is indicated, computed tomography of the thorax (CT thorax) and a full lung function test may be considered. Lung function tests should be performed only when the patient is no longer infectious.	V	D	Weak Good Practice	N
5	Patients with COVID-19 and Acute Respiratory Distress Syndrome (ARDS) will need longer term follow-up with repeat lung function testing and /or radiological imaging at appropriate intervals depending on their clinical status.	V	D	Weak Good Practice	N







In severe disease, further evaluation and longer term follow-up may be required. This may include CT thorax and a full lung function test. Repeat lung function testing and /or radiological imaging at appropriate intervals may be performed depending on their clinical status.

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NEUROLOGY RECOMMENDATIONS FOR COVID-19 PATIENTS

Summary: Stroke in COVID-19 patients

	Different stroke subtypes (e.g. ischemic stroke, haemorrhagic stroke, cerebrovenous thrombosis) have been reported in patients with COVID-19 infection. Stroke can occur during the acute COVID-19 hospitalisation and weeks and months following COVID-19 recovery.
	Ischemic stroke patients with a history of COVID-19 infection who present early should be considered for intravenous recombinant tissue plasminogen activator (TPA) and endovascular treatment.
	Acute stroke treatment (intravenous TPA and endovascular treatment) should not be delayed by the need to await COVID-19 serology and RNA results.
	Stroke patients with a history of COVID-19 infection will benefit from intensive care monitoring (e.g. endotracheal intubation and mechanical ventilation), interventions (e.g. external ventricular drainage, decompression hemicraniectomy and ventriculoperitoneal shunt) and rehabilitation as clinically indicated.
	Depending on investigational findings of stroke mechanisms, antiplatelet or anticoagulation may be prescribed for secondary stroke prevention in ischemic stroke patients with a history of COVID-19 infection.
	Not all ischemic stroke patients with a history of COVID-19 infection require long-term oral anticoagulation.

COVID-19 Clinical Management Recommendations by Neurology

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
1	Different stroke subtypes (e.g. ischemic stroke, haemorrhagic stroke, cerebrovenous thrombosis) have been reported in patients with COVID-19 infection. Stroke can occur during the acute COVID-19 hospitalisation and weeks and months following COVID-19 recovery.	II	B	Strong	Y
2	Ischemic stroke patients with a history of COVID-19 infection who present early should be considered for intravenous recombinant tissue plasminogen activator (TPA) and endovascular treatment.	IV	C	Moderate	Y
3	Acute stroke treatment (intravenous TPA and endovascular treatment) should not be delayed by the need to await COVID-19 serology and RNA results.	IV	C	Moderate	Y
4	Stroke patients with a history of COVID-19 infection will benefit from intensive care monitoring (e.g. endotracheal intubation and mechanical ventilation), interventions (e.g. external ventricular drainage, decompression hemicraniectomy and ventriculoperitoneal shunt) and rehabilitation as clinical indicated.	IV	C	Moderate	Y

5	Depending on investigational findings of stroke mechanisms, antiplatelet or anticoagulation may be prescribed for secondary stroke prevention in ischemic stroke patients with a history of COVID-19 infection.	IV	C	Moderate	Y
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Discussion

Recommendation 1:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
1	Different stroke subtypes (e.g. ischemic stroke, haemorrhagic stroke, cerebrovenous thrombosis) have been reported in patients with COVID-19 infection. Stroke can occur during the acute COVID-19 hospitalisation and weeks and months following COVID-19 recovery.	II	B	Strong	Y

Ischemic stroke^{1,2}, haemorrhagic stroke² and cerebrovenous thrombosis^{2,3} have been reported in patients during the acute and delayed phases following COVID-19 infection. Cases of stroke following COVID-19 have been similarly reported in Singapore^{3,4}.

Recommendation 2:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
2	Ischemic stroke patients with a history of COVID-19 infection who present early should be considered for intravenous recombinant tissue plasminogen activator (TPA) and endovascular treatment.	IV	C	Moderate	Y

Maximal benefits of acute reperfusion treatment take place when TPA and endovascular treatment are administered early. Overwhelming data suggest ischemic stroke patients with previous COVID-19 infection continue to benefit from these treatments^{5,6}.

Recommendation 3:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
3	Acute stroke treatment (intravenous TPA and endovascular treatment) should not be delayed by the need to await COVID-19 serology and RNA results.	IV	C	Moderate	Y






Prompt reversal of cerebral ischemia is central to a successful management of a patient with acute ischemic stroke^{5,6}. As these diagnostic results take time, full personal protective equipment should be worn when treating patients with prior diagnosis of COVID-19 infection or suspected exposure to the virus.

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PSYCHIATRY RECOMMENDATIONS FOR COVID-19 PATIENTS

Summary: Psychological and Mental Health in COVID-19 patients

	We recommend considering comprehensive psycho-social care assessment and support to at risk and vulnerable patients inflicted with COVID-19 infection and/or persistent post-acute COVID-19 infection symptoms, including but not limited to elderly, and individuals living alone who may experience barriers to care.
	In patients with acute COVID-19, we recommend referral to the Psychiatric Consultation Liaison multidisciplinary team (Psych CL-MDT) for assessment and management of the following where indicated: <ul data-bbox="379 510 1390 689" style="list-style-type: none">• neuropsychiatric presentations,• psychiatric responses to acute COVID-19 infection and consequences of isolation, quarantine and treatment complications,• acute exacerbation or relapse of pre-existing psychiatric illness in acute COVID infection.
	We recommend that ASQ Toolkit could be used for the acute COVID-19 patient presenting with emotional distress and existential issues, to screen for acute suicide risk, while PHQ-2 could be used for screening of depressive mood.
	For COVID-19 recovered patients with persistent post-acute COVID-19 neuropsychiatric symptoms, we recommend Psychiatric Consultation Liaison multidisciplinary team (Psych CL-MDT) assessment and management.
	Mass psychiatric screening in patients with new COVID-19 infection, or patients who have recovered from COVID-19 infection is not recommended.

1. Neuropsychiatric and Psychological Manifestation in COVID

Patients with COVID-19 should be monitored for neuropsychiatric manifestations both in the acute and long-term. Furthermore, clinicians managing such patients with co-existing psychiatric conditions should be aware of the risk of a relapse of the conditions.

2. Acute phase

2.1 Neuropsychiatric manifestations and sequelae noted in COVID-19

Acute neurological conditions	Acute Psychiatric Symptoms
Delirium and altered consciousness	Acute confusion Agitation
Encephalopathy	Agitation Confusion
Stroke and TIA	Psychosis Hallucinations Agitation
Seizures	Inter and intra-ictal psychosis Confusion
Treatment induced	Psychosis Mania

2.2 Psychological responses

Since the onset of the COVID-19 pandemic in 2019, there has been a variety of mental health consequences in response to it. Some of these consequences have included: stress, depression, anxiety, feelings of panic, feelings of hopelessness, frustration, feelings of desperation, and struggles with suicidal ideation and behaviour, insomnia, irritability, emotional exhaustion, grief, and traumatic stress symptoms¹.

Various studies have also mentioned a direct psychological impact on the vulnerable populations like elderly, migrants, and the frontline workers including the health care staff (Chen et al., 2020c; Yang et al., 2020b). Incidence of depression, anxiety and suicidality have further been reported across many countries, compounded by the effects of the lockdown (Li and Ge et al., 2020).

		Psychiatric Symptoms
Psychiatric disorders	Major depressive disorder	Suicidal ideation, low mood, sleep and appetite disturbances, excessive guilt, poor energy and concentration.
	Anxiety disorders (Panic, GAD, OCD)	-
	Adjustment disorder	-
	Bereavement/Grief	-
	Circadian rhythm disorders	-
	Sleep disorders	-
Psychological responses	“Cabin fever”, loneliness, guilt, anxiety and fear	-

2.3 Long term sequelae

Neuropsychiatric consequences

		Psychiatric symptoms
Neurological conditions	Stroke and TIA	-
	Encephalopathy	-
	Cognitive impairment	Dementia like symptoms
	Chronic Fatigue Syndrome	-
Psychiatric conditions	Major Depressive disorder	-
	Post-traumatic stress disorder	-
	Anxiety Disorder	-
	Panic disorder	-
	Obsessive compulsive disorder	-
	Psychotic disorder	-

In an analysis of COVID-19 adult patients in the TriNetX database, a global health collaborative clinical research platform collecting real-time electronic medical records data from a network of health care organizations. 40,469 patients were diagnosed with COVID-19 among whom 9,086 (22.5%) patients had neuropsychiatric manifestations. The most common neurologic manifestations included headache (3.7%) and sleep disorders (3.4%), encephalopathy (2.3%), stroke and transient ischemic attack (TIA) (1.0%) and 0.6% had seizures. Most common psychiatric manifestations included anxiety and other related disorders (4.6%), mood disorders (3.8%), while 0.2% patients had suicidal ideation. (Nalleballe et al., 2020)

A case review of 153 COVID-19 patients in the UK found 23 patients with altered mental status fulfilled the clinical case definitions for psychiatric diagnoses, and 21 of these were new diagnoses. Ten of 23 patients with neuropsychiatric disorders had new-onset psychosis, six had a neurocognitive (dementia-like) syndrome, and four had an affective disorder. (Aravinthan et al., 2020)

COVID-19 Clinical Management Recommendations by Psychiatry

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
1	We recommend considering comprehensive psycho-social care assessment and support to at risk and vulnerable patients inflicted with COVID-19 infection and/or persistent post-acute COVID-19 infection symptoms, including but not limited to elderly, and individuals living alone who may experience barriers to care.	V	D	Moderate	N
2	In patients with acute COVID-19, we recommend referral to the Psychiatric Consultation Liaison multidisciplinary team (Psych CL-MDT) for assessment and management of the following where indicated: <ul style="list-style-type: none"> • neuropsychiatric presentations, • psychiatric responses to acute COVID-19 infection and consequences of isolation, quarantine and treatment complications, • acute exacerbation or relapse of pre-existing psychiatric illness in acute COVID infection. 	III	B	Strong	N (case series in preparation)
3	We recommend that ASQ Toolkit could be used for the acute COVID-19 patient presenting with emotional distress and existential issues, to screen for acute suicide risk, while PHQ-2 could be used for screening of depressive mood.	V	D	Moderate	N
4	For COVID-19 recovered patients with persistent post-acute COVID-19 neuropsychiatric symptoms, we	IV	C	Moderate	N

	recommend Psychiatric Consultation Liaison multidisciplinary team (Psych CL-MDT) assessment and management of persisting neuropsychiatric presentations and persistent post-acute COVID-19 symptoms arising from COVID-19 infection.				
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Discussion

Recommendation 1:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
1	We recommend considering comprehensive psycho-social care assessment and support to at risk and vulnerable patients inflicted with COVID-19 infection and/or persistent post-acute COVID-19 infection symptoms, including but not limited to elderly, and individuals living alone who may experience barriers to care.	V	D	Moderate	N

COVID-19 exerts significant psychosocial stress on patients, especially for at-risk and vulnerable patient populations include:

- a. Staying alone with risk of self-care neglect
- b. Elderly
- c. Nursing home residents
- d. Migrant worker with limited in-country social support; presenting with suicidal ideation, low mood, sleep and appetite disturbances, excessive guilt, poor energy and concentration.

The psychosocial needs cannot be underestimated and require deliberate systematic efforts to support the psychological health of these patients.

Recommendation 2:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
2	<p>In patients with acute COVID-19, we recommend referral to the Psychiatric Consultation Liaison multidisciplinary team (Psych CL-MDT) for assessment and management of the following where indicated:</p> <ul style="list-style-type: none"> • neuropsychiatric presentations, • psychiatric responses to acute COVID-19 infection and consequences of isolation, quarantine and treatment complications, • acute exacerbation or relapse of pre-existing psychiatric illness in acute COVID infection. 	III	B	Strong	N (case series in preparation)

For acute management of COVID-19 infection, we recommend Psychiatric Consultation Liaison multidisciplinary team (Psych CL-MDT) management, where indicated:

- a. To assess and manage neuropsychiatric presentations in acute COVID-19 infection, including:
 - Insomnia
 - Impaired attention and concentration
 - Memory impairment
 - Agitation
 - Anxiety
 - Depressed mood
 - Hallucination
 - Confusion
 - Altered consciousness
 - Suicidal ideation

- b. To assess and manage psychiatric responses to acute COVID-19 infection and consequences of isolation, quarantine and treatment complications, including:
 - Boredom and restlessness
 - Agitation
 - Lethargy and fatigue
 - Guilt
 - Anxiety
 - Depressed mood

- Psychosis
 - Suicidal ideation
- c. To assess and manage acute exacerbation or relapse of pre-existing psychiatric illness in acute COVID-19 infection, including:
- Anxiety disorder
 - Affective disorder
 - Schizophrenia
 - OCD
 - Past traumatic stress disorder
 - Psychoactive substance abuse
 - Pre-morbid personality disorder
 - Psychologically at risk and individual with special needs

Recommendation 3:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
3	We recommend that ASQ Toolkit could be used for the acute COVID-19 patient presenting with emotional distress and existential issues, to screen for acute suicide risk, while PHQ-2 could be used for screening of depressive mood.	V	D	Moderate	N

- a. There is no clear evidence of benefit of a mass psychiatric screening in patient with new COVID-19 infection or in patient recovered from COVID-19 infection. But from clinical history and clinical examination, attending EMD or ID Physicians could be alerted to the need for a psychiatric assessment referral.
- b. ASQ Toolkit could be used for acute COVID-19 Patient presenting with emotional distress and existential issues, to screen for acute suicide risk in at risk patients.
- c. PHQ-2 could be used by Attending Physician for the screening depressive mood, and if positive to proceed to PHQ-9 profiling before referring to Psychiatrist.

Recommendation 4:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
4	For COVID-19 recovered patients with persistent post-acute COVID-19 neuropsychiatric symptoms, we recommend Psychiatric Consultation Liaison multidisciplinary team (Psych CL-MDT) assessment and management of persisting neuropsychiatric presentations and persistent post-acute COVID-19 symptoms arising from COVID-19 infection.	IV	C	Moderate	N

For COVID-19 recovered patients with persistent post-acute COVID-19 neuropsychiatric symptoms, we recommend Psychiatric Consultation Liaison multidisciplinary team (Psych CL-MDT) assessment and management of persisting neuropsychiatric presentations arising from COVID-19 infection, and persistent post-acute COVID-19 symptoms, which may include:

- Insomnia, circadian rhythm change
- Cognitive impairment
- Chronic fatigue syndrome
- Adjustment disorder
- Major depressive disorder
- Post-traumatic stress disorder
- Panic disorder
- Obsessive compulsive disorder
- Psychotic disorder
- Suicidal ideation
- Lifestyle changes (weight gain, increased alcohol and tobacco use)
- Exacerbation of dysfunction arising from pre-morbid personality disorder

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**RECOMMENDATIONS FOR CARE OF PAEDIATRIC COVID-19
PATIENTS**

Summary: Paediatric care in COVID-19

	In the current pandemic setting, all children with Kawasaki Disease/ MIS-C should be tested for COVID-19 both by PCR and by serology
	Children hospitalized with COVID-19 should have a full blood count (FBC) and liver function tests (LFTs) performed, while other tests (e.g. C-reactive protein [CRP], lactate dehydrogenase [LDH], chest X-ray [CXR]) may be performed if clinically indicated. Computed tomography (CT) of the chest should not be routinely performed and done only if clinically indicated.
	Children hospitalized with COVID-19 should have routine psychosocial assessment.
	Children with COVID-19 should be assessed for the development of Kawasaki's Disease / Multisystem Inflammatory Syndrome in Children (MIS-C) by WHO criteria.
	Infants with COVID-19 should be with a familiar caregiver during hospital isolation. Older children who are assessed to have sufficient maturity and independence should be counselled for separation from non-COVID-19 infected parents. The management of younger children should take into account his/her level of maturity and independence.
	Infants who are breastfed should continue to do so with appropriate infection prevention and control (IPC) measures in place, unless mothers are too unwell to breastfeed or choose not to, regardless of whether mothers or their infants have suspected or confirmed COVID-19 infection. IPC measures would include wearing of surgical masks, as well as good hand hygiene and sanitation practices.
	Children with clinically significant or worsening COVID-19 pulmonary or systemic disease should be given oxygen and/ or supportive treatment; dexamethasone can be considered in children who require oxygen.
	Children discharged with COVID-19 who are incontinent/wearing diapers and attending preschool/childcare centre/other school, should receive leave of absence from school for up to 6 weeks from time of diagnosis or onset of illness, whichever is earlier.

COVID-19 Clinical Management Recommendations for Paediatric Care

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
1	In the current pandemic setting, all children with Kawasaki Disease/ MIS-C should be tested for COVID-19 both by PCR and by serology	V	D	Weak	N
2	Children hospitalized with COVID-19 should have a full blood count (FBC) and liver function tests (LFTs) performed, while other tests (e.g. C-reactive protein [CRP], lactate dehydrogenase [LDH], chest X-ray [CXR]) may be performed if clinically indicated. Computed tomography (CT) of the chest should not be routinely performed and done only if clinically indicated.	IV	C	Moderate	Y
3	Children hospitalized with COVID-19 should have routine psychosocial assessment.	V	D	Weak	Y
4	Children with COVID-19 should be assessed for the development of Kawasaki's Disease (KD) / Multisystem Inflammatory Syndrome in Children (MIS-C) by WHO criteria.	IV	C	Moderate	N
5	Infants with COVID-19 should be with a familiar caregiver during hospital isolation. Older children who are assessed to have sufficient maturity and independence should be counselled for separation from non-COVID-19 infected parents. The	IV	C	Moderate	Y

	management of younger children should take into account his/her level of maturity and independence.				
6	Infants who are breastfed should continue to do so with appropriate infection prevention and control (IPC) measures in place, unless mothers are too unwell to breastfeed or choose not to, regardless of whether mothers or their infants have suspected or confirmed COVID-19 infection. IPC measures would include wearing of surgical masks, as well as good hand hygiene and sanitation practices.	IV	C	Moderate	Y
7	Children with clinically significant or worsening COVID-19 pulmonary or systemic disease should be given oxygen and/ or supportive treatment; dexamethasone can be considered in children who require oxygen.	V	D	Weak	N
8	Children discharged with COVID-19 who are incontinent/wearing diapers and attending preschool/childcare centre/other school, should receive leave of absence from school for up to 6 weeks from time of diagnosis or onset of illness, whichever is earlier).	V	D	Weak	N

Discussion

Recommendation 1:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
1	In the current pandemic setting, all children with Kawasaki Disease/ MIS-C should be tested for COVID-19 both by PCR and by serology	V	D	Weak	N

KD/MIS-C has been reported in children with COVID-19. In a pandemic setting, COVID-19 should be excluded in children with KD/MIS-C.

Recommendation 2:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
2	Children hospitalized with COVID-19 should have a full blood count (FBC) and liver function tests (LFTs) performed, while other tests (e.g. C-reactive protein [CRP], lactate dehydrogenase [LDH], chest X-ray [CXR]) may be performed if clinically indicated. Computed tomography (CT) of the chest should not be routinely performed and done only if clinically indicated.	IV	C	Moderate	Y

Up to 18-28% of local paediatric patients have documented cytopenia/ deranged liver function tests. Should hospitalization be required, it is good clinical practice to evaluate the above.

Recommendation 3:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
3	Children hospitalized with COVID-19 should have routine psychosocial assessment.	V	D	Weak	Y

The psychosocial should be done together with caregivers/parents in the context of the psychosocial well-being of the family.

Recommendation 4:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
4	Children with COVID-19 should be assessed for the development of Kawasaki's Disease (KD) / Multisystem Inflammatory Syndrome in Children (MIS-C) by WHO criteria.	IV	C	Moderate	N

KD/MIS-C has been reported in children with COVID-19. Where diagnosed, management should be based on Kawasaki Disease treatment guidelines. This entails the use of intravenous immunoglobulin (IVIG), corticosteroids and/or other immunomodulatory therapies. As for resistant KD, there are no specific recommendation for other therapies, e.g. IL-6 inhibitors.

Recommendation 5:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
5	Infants with COVID-19 should be with a familiar caregiver during hospital isolation. Older children who are assessed to have sufficient maturity and independence should be counselled for separation from non-COVID-19 infected parents. The management of younger children should take into account his/her level of maturity and independence.	IV	C	Moderate	Y

The final arrangement for each child is case-dependent, taking into account his/her level of maturity and independence. The familial context and the caregiver/parent should also be considered.

Recommendation 6:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
6	Infants who are breastfed should continue to do so with appropriate infection prevention and control (IPC) measures in place, unless mothers are too unwell to breastfeed or choose not to, regardless of whether mothers or their infants have suspected or confirmed COVID-19 infection. IPC measures would include wearing of surgical masks, as well as good hand hygiene and sanitation practices.	IV	C	Moderate	Y

Breastfeeding should continue where possible and follow the World Health Organisation recommendations.

Recommendation 7:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
7	Children with clinically significant or worsening COVID-19 pulmonary or systemic disease should be given oxygen and/ or supportive treatment; dexamethasone can be considered in children who require oxygen.	V	D	Weak	N

Supportive treatment should be rendered as required, while therapeutic agents with evidence of possible benefit (e.g. dexamethasone) may be considered in severe disease. Appropriate specialists should be consulted for use of these therapeutic agents.

Recommendation 8:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
8	Children discharged with COVID-19 who are incontinent/wearing diapers and attending preschool/childcare centre/other school, should receive leave of absence from school for up to 6 weeks from time of diagnosis or onset of illness, whichever is earlier).	V	D	Weak	N

Stool shedding of SARS-CoV-2 RNA can persist for at least 4-6 weeks after infection. Infectivity of this shedding is unknown and faecally incontinent children should avoid childcare centres or schools to prevent onward transmission.




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**RECOMMENDATIONS FOR CARE OF GERIATRIC COVID-19
PATIENTS**

Summary: Geriatric and palliative care in COVID-19

	Older patients with COVID-19 may present atypically. Hence, diagnostic tests should be administered if suspicion is high based on epidemiological risk factors, even if they are not showing clinical symptoms of COVID-19.
	During periods of society-wide activity restriction, older patients may be at risk of social isolation and experience barriers to healthcare. Healthcare providers should take steps to ensure that their health needs continue to be met, which may include telemedicine, home visits and home delivery of medications.
	Good palliative care should be provided in severe COVID-19, including end-of-life planning. As isolation may exacerbate grief and bereavement, palliative care should include empathetic communication with next-of-kin.

COVID-19 Clinical Management Recommendations for Geriatric and Palliative Care

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
1	Older patients with COVID-19 may present atypically. Hence, diagnostic tests should be administered if suspicion is high based on epidemiological risk factors, even if they are not showing clinical symptoms of COVID-19.	V	D	Weak	N
2	During periods of society-wide activity restriction, older patients may be at risk of social isolation and experience barriers to healthcare. Healthcare providers should take steps to ensure that their health needs continue to be met, which may include telemedicine, home visits and home delivery of medications.	V	D	Weak	N
3	Good palliative care should be provided in severe COVID-19, including end-of-life planning. As isolation may exacerbate grief and bereavement, palliative care should include empathetic communication with next-of-kin.	V	D	Weak	N

Discussion

Recommendation 1:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
1	Older patients with COVID-19 may present atypically. Hence, diagnostic tests should be administered if suspicion is high based on epidemiological risk factors, even if they are not showing clinical symptoms of COVID-19.	V	D	Weak	N

Older persons may present atypically and may have non-specific symptoms. There may not be significant respiratory symptoms or pyrexia despite being infected. COVID-19 should be excluded where there are epidemiological risk factors present.

Appropriate local hospital-based strategies to prevent delirium and deconditioning in older patients admitted with COVID 19 should be instituted as early as possible e.g. reality orientation and early mobilization.

Recommendation 2:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
2	During periods of society-wide activity restriction, older patients may be at risk of social isolation and experience barriers to healthcare. Healthcare providers should take steps to ensure that their health needs continue to be met, which may include telemedicine, home visits and home delivery of medications.	V	D	Weak	N

The healthcare of older patients should ideally be regularly monitored during periods of national lockdown and/or social distancing. Healthcare providers must take all necessary steps to ensure the availability of consult services preferably via telemedicine.

During periods of isolation and social distancing, healthcare providers should ensure that all older patients have access to adequate nutrition, medications and healthcare services. Where required, referral for support services such as through AIC may be considered.

Recommendation 3:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
3	Good palliative care should be provided in severe COVID-19, including end-of-life planning. As isolation may exacerbate grief and bereavement, palliative care should include empathetic communication with next-of-kin.	V	D	Weak	N

Advance Care Plans (especially do-not-resuscitate status and/or extent of care) should be discussed with patients (if possible) and next-of-kin as early as possible as patients may lose their capacity to make decisions in the event the severity of disease increases.

Communications about patient's condition is important. For patients with severe disease, it is important to communicate to next-of-kin early and clearly about the prognosis of the patient whilst acknowledging that the team is doing their best and hoping that patient will recover.






Grief and bereavement management is potentially challenging in patients with COVID as a result of isolation policies, visitation restrictions and the sudden deterioration in health status. Good palliation of symptoms and empathetic communication may mitigate the severity of grief and bereavement in next-of-kin.

All families and/or next-of-kin should be given information of support services within and without the healthcare environment (family service centre, social worker) if they have difficulty coping with the post bereavement period.

On palliation of symptoms, distressing symptoms such as breathlessness maybe be common in patients with COVID-19. Palliation is important for these patients; opioids are safe when they are used judiciously to control symptoms.

**RECOMMENDATIONS FOR CARE OF PREGNANT COVID-19
PATIENTS**

Summary: Obstetric Care in COVID-19 Pregnant Women

	Infected pregnant women have increased risk of developing more severe illness compared to non-pregnant woman. All infected pregnant women should be assessed by multidisciplinary healthcare team to assess risks to both mother and foetus. Monitoring including oxygen saturation, standard blood tests, chest X-rays and foetal scans can be safely used.
	There has been an observed increase in the risk of premature labour in pregnant women with COVID 19. The decision on timing and mode of delivery will need to be individually assessed based on maternal and foetal medical condition.
	There is a small possibility of the virus passing from the mother to the baby in the womb or upon birth (vertical transmission) but the risk is very low, and the majority of infected babies have very mild symptoms
	There has been no evidence of increased stillbirth, neonatal death or congenital malformations in babies of women with COVID-19.
	The rate of neonatal COVID-19 infection is no greater with vaginal deliveries compared to caesarean deliveries. Therefore, COVID-19 should not be a specific indication for caesarean birth and usual obstetric indications for caesarean deliveries should apply.

COVID-19 Obstetric Clinical Management Recommendations

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
1	Infected pregnant women have increased risk of developing more severe illness compared to non-pregnant woman. All infected pregnant women should be assessed by multidisciplinary healthcare team to assess risks to both mother and foetus. Monitoring including oxygen saturation, standard blood tests, chest X-rays and foetal scans can be safely used.	IV	D	Weak	N
2	There has been an observed increase in the risk of premature labour in pregnant women with COVID 19. The decision on timing and mode of delivery will need to be individually assessed based on maternal and foetal medical condition.	IV	D	Weak	N
3	There is a small possibility of the virus passing from the mother to the baby in the womb or upon birth (vertical transmission) but the risk is very low, and the majority of infected babies recover well.	IV	D	Weak	N
4	There has been no evidence of increased stillbirth, neonatal death or congenital	IV	D	Weak	N

	malformations in babies of women with COVID19.				
5	The rate of neonatal COVID-19 infection is no greater with vaginal deliveries compared to caesarean deliveries. Therefore, COVID-19 should not be a specific indication for caesarean birth and usual obstetric indications for caesarean deliveries should apply	IV	D	Moderate	N




For further details on the obstetric recommendations, please refer to the committee opinion developed by the College of Obstetricians & Gynaecologists, *Singapore on Management of Pregnancy and Birth in Women with Coronavirus Diseases (COVID-19)* which was published in April 2020.

Reference

College of Obstetricians & Gynaecologists, Singapore. (2020). *Committee Opinion: Management of Pregnancy and Birth in Women with Coronavirus Diseases (COVID-19)*. Academy of Medicine, Singapore.

**RECOMMENDATIONS FOR PATIENTS WITH PERSISTENT POST
ACUTE COVID-19**

Summary: Persistent post-acute COVID-19 symptoms in recovered COVID-19 patients

	<p>Chronic symptoms have been reported in recovered COVID-19 patients, and include fatigue, cough, shortness of breath, headache/body ache, diarrhoea, nausea, chest/abdominal pain and confusion.</p> <p>These symptoms may be due to organ injury from COVID infection, post viral chronic fatigue syndrome, neurological dysfunction or psychological syndromes.</p> <p>We recommend opportunistic screening of these symptoms in recovered patients.</p>
	<p>In patients who have these symptoms, there should be appropriate assessment and initial symptomatic treatment and monitoring by primary care providers, with escalation of care to relevant multidisciplinary specialties if necessary, to determine diagnosis and management of organ injury, chronic fatigue syndrome (myalgic encephalomyelitis), dysautonomia, cognitive disturbance or psychological syndromes.</p>
	<p>This entity remains undefined in our population. We recommend further research into the surveillance for prevalence and severity of lingering COVID symptoms in our recovered patients.</p>

COVID-19 Clinical Management Recommendations on Persistent Post-Acute COVID-19 Symptoms

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
1	<p>Chronic symptoms have been reported in recovered COVID-19 patients, and include fatigue, cough, shortness of breath, headache/body ache, diarrhoea, nausea, chest/abdominal pain and confusion.</p> <p>These symptoms may be due to organ injury from COVID infection, post viral chronic fatigue syndrome, neurological dysfunction or psychological syndromes.</p> <p>We recommend opportunistic screening of these symptoms in recovered patients.</p>	V	D	Weak	N
2	<p>In patients who have these symptoms, there should be appropriate assessment and initial symptomatic treatment and monitoring by primary care providers, with escalation of care to relevant multidisciplinary specialties if necessary, to determine diagnosis and management of organ injury, chronic fatigue syndrome (myalgic encephalomyelitis), dysautonomia, cognitive disturbance or psychological syndromes.</p>	V	D	Weak	N
3	<p>This entity remains undefined in our population. We recommend further research into the surveillance for prevalence and severity of lingering COVID symptoms in our recovered patients.</p>	V	D	Weak	N

Discussion

Recommendation 1:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
1	<p>Chronic symptoms have been reported in recovered COVID-19 patients, and include fatigue, cough, shortness of breath, headache/body ache, diarrhoea, nausea, chest/abdominal pain and confusion.</p> <p>These symptoms may be due to organ injury from COVID infection, post viral chronic fatigue syndrome, neurological dysfunction or psychological syndromes.</p> <p>We recommend opportunistic screening of these symptoms in recovered patients.</p>	V	D	Weak	N

Persistent post-acute COVID-19 symptoms have been reported, with some coining it as “long-haul COVID-19”. Chronic symptoms have been reported to persist beyond what is generally expected of an acute viral infection, which may entail fatigue, cough, shortness of breath, headache/body ache, diarrhoea, nausea, chest/abdominal pain and confusion.

Please also see the table on screening guidance under recommendation 2.

Recommendation 2:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
2	In patients who have these symptoms, there should be appropriate assessment and initial symptomatic treatment and monitoring by primary care providers, with escalation of care to relevant multidisciplinary specialties if necessary, to determine diagnosis and management of organ injury, chronic fatigue syndrome (myalgic encephalomyelitis), dysautonomia, cognitive disturbance or psychological syndromes.	V	D	Weak	N

Appropriate assessment and work-up should be performed by providers who pick up patients with persisting symptoms after COVID-19 infection. Based on the clinical assessment, appropriate referrals may be made to the relevant specialties as necessary. A suggested approach is tabulated below.

Table: Screening guidance and suggestion for referral

Recommended Symptom to Screen	Comments
Exertional Dyspnoea	Exertional dyspnoea should be graded by the New York Heart Association classification. A cardiovascular and respiratory examination should be performed, and a CXR and/or an ECG may be done as appropriate. Consider referral to Cardiology or Respiratory Medicine as appropriate.
Chest pain/ chest discomfort, non-musculoskeletal	
Cough, chronic	
Cognitive impairment	This may include difficulty remembering, mental concentration, learning new things or task performance Consider referral to Neurology or Psychiatry after excluding organic cause.
Mood disorders - anxiety/ depression	Assess suicide risks. Perform medical evaluation Consider referral to Psychiatry based on severity as appropriate.
Fatigue	Patient should be evaluated for medical causes as well as psychosocial factors. Consider referral to specialty as appropriate.

Recommendation 3:

SN	Recommendation	Level of Evidence	Grade of Evidence	Strength of Recommendation	Supported by Local Evidence?
3	This entity remains undefined in our population. We recommend further research into the surveillance for prevalence and severity of lingering COVID symptoms in our recovered patients.	V	D	Weak	N

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	4	A/Prof Tan Thuan Tong	Senior Consultant & Head, Infectious Diseases, SGH
	5	A/Prof Helen Oh	Senior Consultant, Infectious Diseases, CGH
	6	A/Prof Hsu Li Yang	Vice Dean (Global Health), SSHSPH Consultant, ACE Public Health & Surveillance
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	9	A/Prof Phoa Lee Lan	Senior Consultant, Respiratory & Critical Care Head of Department, Dept of General Medicine, KTPH
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	16	Dr Yap Eng Soo	Senior Consultant, Dept of Haematology-Oncology, NCIS
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Internal Medicine	21	A/Prof Melvin Chua	Senior Consultant & Head, Dept of General Medicine, SKGH
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	23	Adj Asst Prof Mok Yee Ming	Senior Consultant & Chief, Dept of Mood and Anxiety; Regional Chief, Central Region, IMH
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	25	Adj A/Prof Ian Leong	Deputy Divisional Chairman, Integrative & Community Care Clinical Director, Division for Central Health Senior Consultant, TTSH
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