Clinical Management of Patients with COVID-19 – 2nd Interim Guidance

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Acknowledgments

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Preamble

This guidance has been adapted for Canadian use from the WHO document entitled *Clinical management of COVID-19* **–** *Interim guidance - 27 May 2020*. (Available from: https://apps.who.int/iris/handle/10665/332196).

This guidance is informed by currently available scientific evidence, expert opinion, and a multidisciplinary panel of health care providers with experience in the clinical management of patients with COVID-19 and other viral infections (including other severe respiratory infections due to coronaviruses such as SARS and MERS) as well as sepsis and acute respiratory distress syndrome (ARDS). [1] [2] The information presented is subject to change as new information becomes available.

This guidance provides clinicians with interim advice on timely, effective, and safe supportive management of adults, children and youth with suspected or confirmed acute COVID-19. It is not meant to replace clinical judgment or specialist consultation, but rather to strengthen the clinical management of these patients. Best practices for triage and optimized supportive care are included.

In the guidelines, these symbols are used to flag interventions:

- Do – the intervention is beneficial (strong recommendation) **OR** the intervention is a best practice statement
- Don't – the intervention is known to be harmful.
- Consider – the intervention may be beneficial in selected patients (conditional recommendation) **OR** be careful when considering this intervention.

1.0 Background

Coronavirus disease 2019 (COVID-19) is a respiratory tract infection caused by a newly emergent coronavirus that was first recognized in Wuhan, China in December 2019. Genetic sequencing of the virus determined that it is a betacoronavirus closely related to the SARS-CoV-1 virus, named Severe Acute Respiratory Syndrome-related Coronavirus 2 (SARS-CoV-2). [3] [4]

It has been estimated that up to half of persons infected with SARS-CoV-2 will remain pauci-symptomatic or asymptomatic. While most people that develop COVID-19 present with mild or uncomplicated illness, up to 15% of patients may develop severe disease requiring hospitalization and oxygen support and up to 5% may require admission to an intensive care unit (ICU). [5] [4] [6] [7] [8] In severe cases, COVID-19 can be complicated by respiratory failure, acute respiratory distress syndrome (ARDS), sepsis and septic shock, thromboembolism and multiorgan failure, including acute kidney injury and cardiac injury. [9] Older age and co-morbid disease are risk factors for severe disease and death.

Clinical presentation and symptoms of COVID-19 vary in frequency and severity. Symptoms absent at the onset of illness may develop over time with disease progression. Clinical diagnosis should therefore always be confirmed by laboratory testing, and patients should always be encouraged to seek medical consultation if experiencing new or worsening symptoms. [7] [10]

The current estimates of the incubation period range from 1-14 days with median estimates of 5-6 days between infection and the onset of clinical symptoms of the disease. People infected with SARS-CoV-2 may be infectious before symptom onset. [7] The risk of infection from most patients at more than 8 days post symptom onset is likely to be low. [11] [12]

There are few data on the clinical presentation of COVID-19 in specific populations, such as children and pregnant women. Relatively few infant COVID-19 cases have been reported and in children with COVID-19, the symptoms are usually less severe than adults. [7] However, although severe forms of COVID-19 are much less frequent than in adults, many countries have reported some pediatric ICU admissions and deaths related to COVID-19. [13] Clinicians should also be aware of very rare complications that have been associated with COVID-19 infection. A severe multisystem inflammatory syndrome in children (MIS-C) has been reported to share features of typical or atypical Kawasaki disease or toxic shock syndrome. [14] [15] [16] [17] [18] [19] [20] [21] [22]

Pregnant women might be at increased risk for severe COVID-19 illness; experience with severe viral respiratory illness from other etiologies emphasizes the need for unique appreciation of pregnancy-related critical illness. [23]

2.0 Screening and Triage

The primary objective of the COVID-19 response is to slow and stop transmission, find, isolate and test every suspect case, and provide timely, culturally sensitive and appropriate care of patients with COVID-19. The recommended location of care will depend on the patient's severity of illness, patient and cohabitant safety, and patient ability to return to care in the event of worsening illness.

Screening and Triage – Screen and isolate all patients with suspected COVID-19 at the first point of contact with the health care system (such as the emergency department or outpatient department/clinic). Consider COVID-19 as a possible etiology in patients presenting with acute respiratory illness and place all patients suspected to have COVID-19 under Droplet and Contact Precautions, with the addition of Airborne Precautions if performing any aerosol-generating medical procedures. Triage patients using standardized triage tools and manage initial presentations accordingly.

- National surveillance case definitions have been developed to standardize public health reporting. These case definitions, however, are not to be used for clinical purposes. [24]
- Early recognition of suspected patients allows for timely initiation of appropriate infection prevention and control measures (see Section 3.0). Table 1 below outlines the clinical syndromes most often associated with COVID-19.
- Detailed guidance on infection prevention and control in acute healthcare settings and in outpatient and ambulatory care settings is available on the Public Health Agency of Canada website. [25] [26]
- Most people with COVID-19 have uncomplicated or mild illness (approximately 80%). Some will develop severe illness requiring oxygen therapy and up to 5% will develop critical illness requiring ICU treatment. Of those critically ill, many will require mechanical ventilation. [9] [27] [7] [11] [8]
- For those with mild illness, hospitalization is not required unless there is concern about rapid deterioration or inability to return promptly to hospital.
- Isolation is necessary to contain virus transmission. All patients cared for outside of the hospital (i.e.,

at home) should be instructed to follow public health protocols for self-isolation and return to hospital if their symptoms worsen.

- Early identification of those with severe illness or pneumonia, allows for optimized supportive care treatments and safe, rapid referral and admission to a hospital.
- Older people and those with comorbidities (e.g. cardiovascular disease, diabetes mellitus, obesity, pre-existing lung conditions) have increased risk of severe disease and mortality. While they may present with mild disease, they have a higher risk of deterioration and should be monitored closely.
- Goals of care discussions should be a component of care for all patients, especially those who are at risk for, or present with, severe disease. Whether or not patients receive intensive and organ-supportive care in severe illness, patients should receive symptom-based care (including dyspnea management) and palliative care should be offered as appropriate. Symptom-based care and palliative care can be provided alongside supportive and curative treatments, and do not compromise survival.

Table 1 – Clinical Syndromes Associated with COVID-19

Syndrome	Details
Asymptomatic/ presymptomatic	Patients will be tested for SARS-CoV2 and have positive results without ever having symptoms or prior to the development of symptoms. [10]
Mild illness	Patients with uncomplicated upper respiratory tract viral infection typically present with some signs or symptoms of COVID-19 but without shortness of breath or dyspnea or abnormal imaging. These patients may have non-specific symptoms such as fever, fatigue, cough (with or without sputum production), anorexia, malaise, muscle pain, sore throat, dyspnea, nasal congestion, conjunctivitis, loss/alteration of smell and taste, or headache. Patients may also present with diarrhea, abdominal pain, nausea and vomiting. [7] [28] [29] [30] Many are afebrile or have low-grade fever. The elderly and immunocompromised may present with atypical symptoms. Symptoms due to physiologic adaptations of pregnancy or adverse pregnancy events, e.g., dyspnea, fever, GI symptoms or fatigue, may overlap with COVID-19 symptoms.
Pneumonia	***Adult*** with pneumonia but no signs of severe pneumonia and no need for supplemental oxygen. ***Child*** with non-severe pneumonia who has cough or difficulty breathing plus tachypnea (in breaths per minute): < 2 months: ≥ 60; 2–11 months: ≥ 50; 1–5 years: ≥ 40), and no signs of severe pneumonia. While the diagnosis of pneumonia can be made on clinical grounds; chest imaging (radiograph, CT scan, ultrasound) may assist in diagnosis and identify or exclude pulmonary complications.
Severe pneumonia	***Adolescent or adult***: fever or suspected respiratory infection, plus one of the following: respiratory rate > 30 breaths/min; severe respiratory distress; or SpO_2 < 90% on room air (adapted). [31] ***Child*** with cough and/or difficulty in breathing, plus at least one of the following: central cyanosis or SpO_2 < 90%; severe respiratory distress (e.g. grunting, marked chest indrawing); signs of pneumonia with: inability to breastfeed or drink, lethargy or unconsciousness, or convulsions. [32] Other signs of pneumonia may be present: fast breathing (in breaths/min) < 2 months: ≥ 60; 2–11 months: ≥ 50; 1–5 years: ≥ 40. [33] Chest imaging may identify some pulmonary complications.
Acute respiratory distress syndrome (ARDS)	***Onset***: within 1 week of a known clinical insult or new or worsening respiratory symptoms. ***Chest imaging*** (radiograph, CT scan, or lung ultrasound): bilateral opacities, not fully explained by volume overload, lobar or lung collapse, or nodules.

Syndrome	Details
[34] [35] [36]	***Origin of pulmonary infiltrates***: respiratory failure not fully explained by cardiac failure or fluid overload. Need objective assessment (e.g. echocardiography) to exclude hydrostatic cause of infiltrates/edema if no risk factor present. ***Oxygenation impairment in adults***: [34] [36] • mild ARDS: 200 mmHg < PaO_2/FiO_2[a] ≤ 300 mmHg (with PEEP or CPAP ≥ 5 cmH_2O, or non-ventilated) • moderate ARDS: 100 mmHg < PaO_2/FiO_2 ≤ 200 mmHg (with PEEP ≥ 5 cmH_2O, or non-ventilated) • severe ARDS: PaO_2/FiO_2 ≤ 100 mmHg (with PEEP ≥ 5 cmH_2O, or non-ventilated) • when PaO_2 is not available, SpO_2/FiO_2 ≤ 315 suggests ARDS (including in non-ventilated patients) ***Oxygenation impairment in children***: Note OI = Oxygenation Index and OSI = Oxygenation Index using SpO_2. Use PaO_2-based metric when available. If PaO_2 not available, wean FiO_2 to maintain SpO_2 at 92-97% to calculate OSI or SpO_2/FiO_2 ratio: • bilevel NIV or CPAP ≥ 5 cmH_2O via full face mask: PaO_2/FiO_2 ≤ 300 mmHg or SpO_2/FiO_2 ≤ 264 • mild ARDS (invasively ventilated): 4 ≤ OI < 8 or 5 ≤ OSI < 7.5 • moderate ARDS (invasively ventilated): 8 ≤ OI < 16 or 7.5 ≤ OSI < 12.3 • severe ARDS (invasively ventilated): OI ≥ 16 or OSI ≥ 12.3
Multi-system Inflammatory Syndrome in Children (MIS-C)	This is a syndrome that has been described in children and adolescents that presents with hyper-inflammatory markers with features of Kawasaki syndrome or septic shock. It is temporally related to COVID-19 outbreaks in several jurisdictions. Diagnostic criteria and characterization of this syndrome are evolving. A full discussion of this syndrome is beyond the scope of this document.
Sepsis [1] [2]	***Adults***: life-threatening organ dysfunction caused by a dysregulated host response to suspected or proven infection. Signs of organ dysfunction include[b]: altered mental status, difficult or fast breathing, low oxygen saturation, reduced urine output, fast heart rate, weak pulse, cold extremities or low blood pressure, skin mottling, or laboratory evidence of coagulopathy, thrombocytopenia, acidosis, high lactate or hyperbilirubinemia. [37] [1] ***Children***: suspected or proven infection and ≥ 2 age-based systemic inflammatory response syndrome criteria, of which one must be abnormal temperature or white blood cell count for age.
Septic shock [1] [2]	***Adults***: persisting hypotension despite volume resuscitation, requiring vasopressors to maintain MAP ≥ 60-65 mmHg and serum lactate level > 2 mmol/L. ***Children***: any hypotension (SBP < 5th centile or > 2 SD below normal for age) or 2 or 3 of the following: altered mental state; tachycardia or bradycardia (HR < 90 bpm or > 160 bpm in infants and HR < 70 bpm or > 150 bpm in children); prolonged capillary refill (> 2 sec) or weak pulse; tachypnea; mottled or cool skin or petechial or purpuric rash; increased lactate; oliguria; hyperthermia or hypothermia. [38] Children often have tachycardia before rapid onset of hypotension occurs.

Footnotes

a If altitude is higher than 1000m, then correction factor should be calculated as follows: PaO_2/FiO_2 x barometric pressure/760.

b The SOFA score ranges from 0 to 24 and includes points related to six organ systems: respiratory (hypoxemia defined by low PaO_2/FiO_2); coagulation (low platelets); liver (high bilirubin); cardiovascular (hypotension); central nervous system (low level of consciousness defined by Glasgow Coma Scale); and renal (low urine output or high creatinine).

Sepsis is defined by an increase in the sepsis-related SOFA score of ≥ 2 points. Assume the baseline score is 0 if data are not available. [39]

Abbreviations: ARI acute respiratory infection; BP blood pressure; bpm beats per minute; CPAP continuous positive airway pressure; FiO_2 fraction of inspired oxygen; MAP mean arterial pressure; NIV non-invasive ventilation; OI oxygenation Index; OSI oxygenation Index using SpO_2; PaO_2 partial pressure of oxygen; PEEP positive end-expiratory pressure; SBP systolic blood pressure; SD standard deviation; SIRS systemic inflammatory response syndrome; SOFA sequential organ failure assessment; SpO_2 oxygen saturation.

3.0 Infection Prevention and Control Measures

Infection prevention and control (IPC) is a critical and integral part of the clinical management of patients suspected or confirmed to have COVID-19.

Detailed national IPC guidance for COVID-19 in acute health care settings is available from the Public Health Agency of Canada (PHAC). See https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/health-professionals/infection-prevention-control-covid-19-second-interim-guidance.html. Some provinces and territories have also issued IPC guidance for their jurisdiction, which complement existing regional and institutional policies. IPC guidance documents are revised and updated as new evidence becomes available therefore refer to the guidance documents directly.

Every effort should be made to allow support persons and essential visitors to visit patients. This is perhaps particularly important for persons with disabilities and older persons, as well as at-risk patients and those nearing the end of life, in order to support the emotional burden and stress of both patients and loved ones. Visitation may be dependent upon sufficient local supply of PPE and the epidemiology of the virus in the local community. Visitors should receive in-time education, training, and monitoring for compliance with IPC measures, including practice with putting on and taking off appropriate PPE. Institutions will need to ensure that there are policies in place for PPE supply procurement and use. Health care settings should refer to the relevant local and jurisdictional public health guidance.

4.0 Collection of Specimens for Laboratory Diagnosis

Testing criteria recommendations change as the situation evolves in regions. All patients who are clinically suspected of infection with COVID-19 should be tested.

Currently, PCR-based molecular testing is predominantly being used in Canada. Since the sensitivity and specificity are linked to the viral load in the specimen, test performance varies during the course of the illness and by specimen type and quality of specimen collection. The virus is detected at high levels in the upper respiratory tract early in infection, and declines with time, usually over a 7 - 10 day period, although a prolonged period of shedding has been observed in recovering patients. In patients that develop a lower respiratory tract infection, detection from upper respiratory tract specimens (nasopharyngeal or nose/throat specimens) can be variable. In patients who are intubated, a lower respiratory tract specimen should be obtained, if possible. If there is a high suspicion of COVID-19 even after a negative swab of either type, individuals should be re-tested and have imaging of their lungs.

False negative test results/interpretations can occur when:

- The patient was not infected at the time of the initial swab, but became infected from a later exposure.
- The patient is infected but is not yet shedding much virus in the upper respiratory tract. Every infection has a "window period" during which time the virus incubating in the patient may be there in quantities that are too low to be detected by any diagnostic test.
- The patient is shedding virus but the sample collection was poor. Proper collection technique is essential to ensure that an adequate amount of specimen is collected from the correct anatomical site.

- The patient's infection is manifesting outside the upper respiratory tract. In symptomatic people with mild infection, we know that the virus is shed just before or soon after symptom onset and in high numbers in the upper respiratory tract, lasting for at least 5-7 days. [40] However, in patients who have pneumonia, the most sensitive specimen is from the lungs.

While it is very unusual to get a false positive result due to the cross reactivity with another RNA virus, PCR testing can sometimes give non-specific reactions or contamination within the laboratory can occur. Expert interpretation may be required in such cases.

Further guidance on appropriate testing and specimen collection for COVID-19 is available from the Public Health Agency of Canada, the Canadian Public Health Laboratory Network and from provincial/territorial public health laboratories. [10] [41]

Collect specimens for COVID-19 testing as recommended by your local or provincial public health laboratory.

Collect blood cultures for bacteria where clinically indicated based on the presenting syndrome, e.g., sepsis or severe pneumonia, ideally before antimicrobial therapy. DO NOT delay antimicrobial therapy to collect blood cultures. Blood cultures should be done in children if clinically indicated.

- In admitted patients with suspected COVID-19, the diagnosis should be first attempted with an upper respiratory specimen, preferably a nasopharyngeal swab. However, a mid-turbinate and/or throat swab can be collected as an alternative if nasopharyngeal swabs are not available. For admitted patients with suspected COVID-19, if the upper respiratory swab is negative and there remains a high degree of clinical suspicion a repeat swab should be collected. In severely ill patients whose upper respiratory tract specimen is negative but a COVID-19 diagnosis is still suspected, a lower respiratory tract specimen consisting of sputum, or closed system suctioned endotracheal aspirate should also be collected when possible (e.g., if the patient is producing sputum or they are already ventilated). Once a patient has a positive laboratory test, further testing for diagnostic purposes is not necessary. [42]
- Patients can be infected with more than one virus at the same time. Coinfections with other respiratory viruses in people with COVID-19 have been reported. Therefore, identifying infection with one respiratory virus does not exclude SARS-CoV-2 virus infection, and vice-versa.

SARS-CoV-2 antibody tests are not recommended for diagnosis of current SARS-CoV-2 infection, but they may be useful in post-infectious syndromes.

5.0 Management of Mild COVID-19

Patients with mild disease do not require hospitalization, unless there is concern for rapid deterioration or an inability to return promptly to hospital.

Isolation is necessary to contain virus transmission. All patients cared for outside hospital should be instructed to follow public health protocols for self-isolation and return to hospital if symptoms worsen. Self-isolation protocols are available from PHAC and provincial/territorial and local public health departments.

Provide patients with mild COVID-19 information on symptomatic treatment.

✅ **Counsel patients with mild COVID-19 and their caregivers about the signs and symptoms of complications that should prompt urgent care.** If they develop symptoms like difficulty breathing, pain or pressure in the chest, confusion, drowsiness, or weakness, they should seek follow-up care.

- In children signs and symptoms of clinical deterioration requiring urgent re-evaluation include difficulty breathing/fast or shallow breathing (for infants: grunting, inability to breastfeed), blue lips or face, chest pain or pressure, new confusion, inability to awaken/not interacting when awake, inability to drink or keep down liquids, extreme weakness).

❌ **Antibiotics should not be prescribed to patients with suspected or confirmed mild COVID-19 unless there is clinical suspicion of a bacterial infection**.

6.0 Management of Moderate COVID-19

❌ **Patients with moderate suspected or confirmed COVID-19 (i.e. with clinical signs of pneumonia but no signs of severe pneumonia, including SpO2 ≥ 90% on room air) who are not determined to be at high risk of deterioration may not require hospitalization, but they should be isolated.**

- The decision regarding the location of care should be made on a case-by-case basis and will depend on the clinical presentation, requirement for supportive care, potential risk factors for severe disease, and conditions at home, including the presence of vulnerable persons in the household.
- For patients at high risk for deterioration, admission to hospital should be considered.
- The median time to acute respiratory distress syndrome (ARDS) ranges from 8 to 12 days.
- Lymphopenia, neutrophilia, elevated serum alanine aminotransferase and aspartate aminotransferase levels, elevated lactate dehydrogenase, high CRP, and high ferritin levels may be associated with greater illness severity. [43]

❌ **Antibiotics should not be prescribed to patients with suspected or confirmed moderate COVID-19 unless there is clinical suspicion of a bacterial infection.**

7.0 Management of Severe COVID-19

7.1 Oxygen Therapy and Monitoring

✅ **Give supplemental oxygen therapy immediately to patients with COVID-19 who have severe acute respiratory infection and respiratory distress, hypoxaemia or shock, and target saturations of 90-96% SpO_2 during resuscitation.**

- ***Adults*** with a worsening clinical presentation (obstructed or absent breathing, severe respiratory distress, central cyanosis, shock, coma or convulsions) should receive airway management and oxygen therapy. Initiate oxygen therapy at 5 L/min and titrate flow rates to reach target SpO_2 ≥ 94% during resuscitation; or use face mask with reservoir bag (at 10-15 L/min) if the patient is in critical condition. Once the patient is stable, the target is > 90% SpO_2 in non-pregnant adults and ≥ 92–95% in pregnant patients.

- In **adults**, techniques such as positioning, e.g. high supported sitting may help to optimize oxygenation, ease breathlessness and reduce energy expenditure. [44] Prone position for awake, spontaneously breathing patients may also improve oxygenation and the ventilation/perfusion ratio, but evidence is lacking and should be done under clinical trial protocols to assess efficacy and safety. ***Children*** with a worsening clinical presentation (obstructed or absent breathing, severe respiratory distress, central cyanosis, shock, coma or convulsions) should receive airway management and oxygen therapy during resuscitation to target $SpO_2 \geq 94\%$; otherwise, the target SpO_2 is $\geq 90\%$. [45] The use of a nasal cannula is preferred in young children, as it may be better tolerated.
- All areas where patients with severe acute respiratory infection are cared for should be equipped with pulse oximeters, functioning oxygen systems and disposable, single-patient use, oxygen-delivering interfaces (nasal cannula, face mask and mask with reservoir bag).

Closely monitor patients with COVID-19 for signs of clinical deterioration, such as rapidly progressive respiratory failure or shock and respond immediately with supportive care interventions.

- Patients hospitalized with COVID-19 require regular monitoring of vital signs and, where possible, use of early warning scores (e.g. NEWS2) that facilitate early recognition and escalation of care for a deteriorating patient. [46] Deterioration in adults is often sudden and may occur in the second week of illness.
- Patients with COVID-19 who have signs or symptoms suggestive of venous or arterial thromboembolism, (e.g. stroke, deep venous thrombosis, pulmonary embolism or acute coronary syndrome) should be diagnosed (using laboratory tests and/or imaging) and treated according to hospital protocols. In pregnant women, sepsis is harder to assess. Use of a modified sepsis score, such as the modified early assessment warning system (MEOWS) is recommended. [47]
- In adults, a complete blood count with differential, electrolytes, creatinine, liver enzymes, liver function tests and lactate as well as other clinically indicated diagnostics (e.g. blood tests, chest imaging and an ECG), should be performed at admission and as clinically indicated, to monitor for complications such as acute liver injury, acute kidney injury, acute cardiac injury or shock. Paediatric patients should have testing done as indicated by clinical judgement. Consider developing electronic order sets or pre-printed orders.
- Application of timely, effective and safe supportive therapies is the cornerstone of therapy for patients who develop severe manifestations of COVID-19.
- After resuscitation and stabilization of a pregnant patient, fetal well-being should be monitored.

Understand the patient's co-morbid conditions and tailor management accordingly.

- Determine which chronic therapies should be continued and which should be stopped temporarily.
    - Monitor for drug interactions
    - Revisit the need for any held medications when clinically appropriate
- Metered dose inhalers with a spacer are preferred to nebulizers to reduce the potential to generate respiratory aerosols.
- Antihypertensive drugs should not routinely be stopped in patients with COVID-19, but therapy may need to be adjusted based on general considerations for patients with acute illness, with particular reference to maintaining normal blood pressure and renal function.
- Patients with psychiatric and neurological manifestations should be assessed for any underlying causes, including the monitoring of oxygenation and fluid status, correcting metabolic or endocrine abnormalities, addressing co-infections, minimizing the use of medications that may cause or worsen delirium, treating withdrawal from substances, understanding and minimizing the effects of any harmful drug-drug interactions and maintaining normal sleep cycles as much as possible.

- To reduce delirium in patients who are receiving invasive ventilation, consideration should be given to minimize continuous or intermittent sedation, targeting specific titration endpoints (light sedation unless contraindicated) or with daily interruption of continuous sedative infusions.
- In patients experiencing agitation (defined as marked restlessness or excessive motor activity, often accompanied by anxiety), calming communication strategies (to reorient the person) should be attempted. Acute pain due to physical illness or air hunger should be considered as triggers for agitation and need to be addressed immediately. While non-pharmacologic strategies are preferred, in case they are unsuccessful or distress is severe, psychotropic medications may need to be trialed alongside non-pharmacologic interventions.

Use conservative fluid management in patients with severe acute respiratory infection when there is no evidence of shock.

- Patients with severe acute respiratory disease should be treated cautiously with intravenous fluids, because aggressive fluid resuscitation may worsen oxygenation, especially in settings where there is limited availability of mechanical ventilation. [48] This applies to the care of both children and adults.

7.2 Treatment of Co-infections

The prevalence of acute co-infections or secondary infections coinciding with COVID-19 has not been adequately described but appears to be low. [49] Antibiotic overuse increases the risk of emergence and transmission of multidrug-resistant bacteria. Infections with multidrug- resistant bacteria are more difficult to treat and are associated with increased morbidity and mortality.

Give empiric antimicrobials to treat all likely pathogens causing severe acute respiratory infection and sepsis as soon as possible, within 1 hour of initial patient assessment for patients with sepsis.

- Empiric antibiotic treatment should be based on the clinical diagnosis (e.g., community-acquired pneumonia, health care-associated pneumonia or sepsis), local epidemiology and susceptibility data. The Infectious Disease Society of America and the American Thoracic Society have published treatment guidelines for community-acquired pneumonia that can be found at: https://www.idsociety.org/practice-guideline/practice-guidelines/#/name_na_str/ASC/0/+/.

Frequently re-evaluate and de-escalate empiric therapy where possible on the basis of microbiology results and clinical judgment.

- Regularly review the possibility of switching of intravenous to oral route of administration
- If antimicrobials are continued, this should be for the shortest recommended duration (for most indications 5-7 days)
- When there is ongoing local circulation of influenza, empiric therapy with a neuraminidase inhibitor should be considered for the treatment of influenza viruses in patients with or at risk for severe disease. [50]

8.0 Management of Critical COVID-19

8.1 Acute Respiratory Distress Syndrome (ARDS)

Recognize severe hypoxemic respiratory failure when a patient with respiratory distress is failing standard oxygen therapy and prepare to provide advanced oxygen/ventilatory support.

- Patients may continue to have increased work of breathing or hypoxemia even when oxygen is delivered via a face mask with reservoir bag (flow rates of 10–15 L/min, which is typically the minimum flow required to maintain bag inflation; FiO_2 0.60–0.95). Hypoxemic respiratory failure in ARDS commonly results from intrapulmonary ventilation-perfusion mismatch or shunt and usually requires mechanical ventilation. [1]

Endotracheal intubation should be performed by a trained and experienced provider using airborne precautions.

- Patients with ARDS, especially young children or those who are obese or pregnant, may desaturate quickly during intubation. Pre-oxygenate with 100% FiO_2 for 5 minutes, via a face mask with reservoir bag, bag-valve mask. The utilization of video laryngoscopy to increase chance of intubation at first attempt should be considered. Rapid sequence intubation is appropriate after an airway assessment that identifies no signs of difficult intubation, avoiding manual ventilation as a means to avoid aerosol generation, where possible and safe for patient care. [51] [52] [53]

Among hospitalized adult patients who have COVID-19 and require supplemental oxygen or mechanical ventilation, clinicians should strongly consider dexamethasone 6 mg IV daily for 10 days (or until off oxygen or discharge if earlier) or equivalent glucocorticoid dose.

- This guidance is not meant to replace clinical judgment or specialist consultation.
- There are currently no data on the use of dexamethasone in children with severe disease who require supplemental oxygen or mechanical ventilation, hence clinical judgement should be applied if considering its use in this population.

Recommendations for mechanically ventilated adult and pediatric patients with ARDS

Implement mechanical ventilation using lower tidal volumes (4–8 mL/kg predicted body weight [PBW]) and lower inspiratory pressures (plateau pressure < 30 cmH_2O).

- ***Adults –*** This is a strong recommendation from a clinical guideline for patients with ARDS, and is suggested for patients with sepsis-induced respiratory failure who do not meet ARDS criteria. [1] The initial tidal volume is 6 mL/kg PBW; tidal volume up to 8 mL/kg PBW is allowed if undesirable side-effects occur (e.g. dyssynchrony, pH < 7.15). Permissive hypercapnia is permitted. Ventilator protocols are available. [54] The use of deep sedation may be required to control respiratory drive and achieve tidal volume targets.
- ***Children*** **-** A lower level of plateau pressure (< 28 cmH_2O) is targeted, and a lower pH target is permitted (7.15–7.30). Tidal volumes should be adapted to disease severity: 3–6 mL/kg PBW in the case of poor respiratory system compliance, and 5–8 mL/kg PBW with better preserved compliance. [53] Slightly higher Plateau pressures (30-32 cm H_20) can be tolerated in case of poor chest wall compliance.

In adult patients with severe ARDS, prone ventilation for 12- 16 hours per day should be considered.

- Application of prone ventilation should be considered for adult patients, preferably for 16 hours per day, and may be considered for paediatric patients with severe ARDS but requires sufficient human resources

and expertise to be performed safely.[33,34] Protocols (including videos) are available at: *https://www.nejm.org/doi/full/10.1056/NEJMoa1214103*.

- Pregnant women should not be placed in a prone position but in the supine position with a wedge placed under the right hip to decrease aortocaval obstruction, or placed in lateral decubitus position.

Use a conservative fluid management strategy for ARDS patients without tissue hypoperfusion.

- This is a strong recommendation for both adults and children; the main effect is to shorten the duration of ventilation [1]. See reference [55] for a sample protocol.

In patients with moderate or severe ARDS, higher PEEP instead of lower PEEP is suggested.

- PEEP titration requires consideration of benefits (reducing atelectrauma and improving alveolar recruitment) vs risks (end-inspiratory overdistension leading to lung injury and higher pulmonary vascular resistance). Tables are available to guide PEEP titration based on the FiO_2 required to maintain SpO_2. [54] Although high driving pressure (plateau pressure minus PEEP) may more accurately predict increased mortality in ARDS compared with high tidal volume or plateau pressure, data from RCTs of ventilation strategies that target driving pressure are not currently available. [56]
- Recruitment manoeuvres (RMs) can be delivered as episodic periods of high continuous positive airway pressure (CPAP) (30–40 cmH_2O), progressive incremental increases in PEEP with constant driving pressure, or high driving pressure; considerations of benefits vs risks are similar. PEEP and RMs were both conditionally recommended in a clinical practice guideline. For PEEP, the guideline considered an individual patient data meta-analysis of three RCTs. [57] However, a subsequent RCT of high PEEP and prolonged high-pressure RMs showed harm, suggesting that the protocol in this RCT should be avoided. [58] Monitoring of patients to identify those who respond to the initial application of higher PEEP or a different RM protocol, and stopping these interventions in non-responders are suggested, noting that patients with hypoxic respiratory failure without strong suspicion or evidence of alveolar de-recruitment are less likely to benefit from RMs but may still be at risk of side-effects. [59]

In patients with moderate-severe ARDS (PaO_2/FiO_2 < 150), neuromuscular blockade by continuous infusion should not be routinely used.

- While one trial found that this strategy improved survival in adult patients with severe ARDS (PaO_2/FiO_2 < 150) without causing significant weakness, results of a recent larger trial found that use of neuromuscular blockage with high PEEP strategy was not associated with a survival benefit when compared with a light sedation strategy without neuromuscular blockade. [60] [61] Continuous neuromuscular blockade may still be considered in patients, both adults and children, with ARDS in certain situations, such as ventilator dyssynchrony despite sedation, such that tidal volume limitation cannot be reliably achieved; refractory hypoxemia; or hypercapnia.

Avoid disconnecting the patient from the ventilator, which results in loss of PEEP and atelectasis.

Use in-line catheters for airway suctioning and clamp the endotracheal tube when disconnection is required (e.g., transfer to a transport ventilator).

Recommendations for adult and pediatric patients with ARDS who are treated with non-invasive or high flow oxygen systems

High-flow nasal oxygen (HFNO) and non-invasive ventilation (NIV) should be considered.

Patients treated with either HFNO or NIV should be closely monitored for clinical deterioration**.**

- Adult HFNO systems can deliver 60 L/min of gas flow and FiO_2 up to 1.0. Pediatric circuits generally only handle up to 25 L/min, and many children will require an adult circuit to deliver adequate flow.
- Compared with standard oxygen therapy, HFNO reduces the need for intubation. [62] Patients with hypercapnia (exacerbation of obstructive lung disease, cardiogenic pulmonary edema), hemodynamic instability, multiorgan 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. [62] [63] [64] 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 hour). Evidence-based guidelines on the treatment of patients with COVID-19 with HFNO do not exist, and reports on HFNO in other coronavirus-infected patients are limited. [64]
- NIV guidelines make no recommendation for use in hypoxemic respiratory failure (apart from cardiogenic pulmonary edema and post-operative respiratory failure) or pandemic viral illness. [1] Risks include delayed intubation, large tidal volumes, and injurious transpulmonary pressures. Limited data suggest a high failure rate in patients with other viral infections such as MERS who receive NIV. [65]
- Patients receiving a trial of NIV 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 hour). Patients with haemodynamic instability, multiorgan failure, or abnormal mental status should likely not receive NIV in place of other options such as invasive ventilation.
- In situations where mechanical ventilation may not be available, bubble nasal CPAP may be used. for newborns and children with severe hypoxemia. [66]
- Because of uncertainty around the potential for aerosolization, HFNO, NIV, including bubble CPAP, should be used with airborne precautions until further evaluation of safety can be completed. If these interventions are performed outside of private rooms in ICUs with appropriate ventilation systems installed, then cohorting of patients requiring these interventions in designated wards, where possible, will facilitate the implementation of airborne precautions. All staff entering in the immediate vicinity of patients receiving potentially aerosol generating medical procedures must wear PPE appropriate for the procedures.

Recommendations for adult and paediatric patients with ARDS in whom a lung protective ventilation strategy fails

In settings with access to expertise in extracorporeal membrane oxygenation (ECMO), consider referral of patients who have refractory hypoxemia despite lung protective ventilation.

- An RCT of ECMO for adult patients with ARDS was stopped early and found no statistically significant difference in the primary outcome of 60-day mortality between ECMO and standard medical management (including prone positioning and neuromuscular blockade). [67] However, ECMO was associated with a reduced risk of the composite outcome of mortality and crossover to ECMO, and a post hoc Bayesian analysis of this RCT showed that ECMO is very likely to reduce mortality across a range of prior assumptions. [67] [68] In patients with MERS, ECMO vs conventional treatment was associated with reduced mortality in a cohort study. [69] ECMO should ideally be offered in expert centres with a sufficient case volume to maintain expertise and that can apply the IPC measures required for adult and pediatric COVID-19 patients. [70] [71]

8.2 Septic Shock

Recognize septic shock in adults when infection is suspected or confirmed AND vasopressors are needed to maintain mean arterial pressure (MAP) ≥ 60-65 mmHg AND lactate is ≥ 2 mmol/L, in absence of hypovolemia.

Recognize septic shock in children with any hypotension (systolic blood pressure [SBP] < 5th centile or 2 SD below normal for age) or two or more of the following: altered mental state; bradycardia or tachycardia (HR < 90 bpm or > 160 bpm in infants and HR < 70 bpm or > 150 bpm in children); prolonged capillary refill (> 2 sec) or feeble pulses; tachypnea; mottled or cool skin or petechial or purpuric rash; increased lactate; oliguria; hyperthermia or hypothermia.

- In the absence of a lactate measurement, use blood pressure (i.e. MAP) and clinical signs of perfusion to define shock.
- Standard care includes early recognition and the following treatments within 1 hour of recognition: antimicrobial therapy and initiation of fluid bolus and vasopressors for hypotension. [1] The use of central venous and arterial catheters should be based on resource availability and individual patient needs. Detailed guidelines are available for the management of septic shock in adults and children. [1] [2] [33] Alternate fluid regimens are suggested when caring for adults and children in resource-limited settings. [72] [73]

Recommendations for resuscitation strategies for adult and paediatric patients with septic shock.

In resuscitation for septic shock in *adults*, give 250-500 mL crystalloid fluid as a rapid bolus in the first 15-30 minutes and reassess for signs of fluid overload after each bolus.

In resuscitation for septic shock in *children*, give 10-20 mL/kg crystalloid fluid as a rapid bolus in the first 30-60 minutes and reassess for signs of fluid overload after each bolus.

Fluid resuscitation may lead to volume overload, including respiratory failure, particularly with ARDS. If there is no response to fluid loading or signs of volume overload appear (e.g. jugular venous distension, crackles on lung auscultation, pulmonary edema on imaging, or hepatomegaly in children), then reduce or discontinue fluid administration. This step is particularly important in patients with hypoxemic respiratory failure.

- Crystalloids include normal saline and Ringer's lactate, with a preference for Ringer's lactate.
- Determine need for additional fluid boluses (500-1000 mL in adults or 10–20 mL/kg in children) based on clinical response and improvement of perfusion targets. Perfusion targets include MAP (≥ 60-65 mmHg or age-appropriate targets in children), urine output (> 0.5 mL/kg/hr in adults, 1 mL/kg/hr in children), and improvement of skin mottling and extremity perfusion, capillary refill, heart rate, level of consciousness, and lactate.
- Consider dynamic indices of volume responsiveness to guide volume administration beyond initial resuscitation based on local resources and experience. [1] These indices include passive leg raises, fluid challenges with serial stroke volume measurements, or variations in systolic pressure, pulse pressure,

inferior vena cava size, or stroke volume in response to changes in intrathoracic pressure during mechanical ventilation.

- In pregnant women, compression of the inferior vena cava can cause a decrease in venous return and cardiac preload and may result in hypotension. For this reason, pregnant women should be cared for with a wedge under their right hip and may need to be placed in a lateral decubitus position to off-load the inferior vena cava. [74]
- Clinical trials conducted in resource limited settings comparing aggressive versus conservative fluid regimens suggest higher mortality in patients treated with aggressive fluid regimes for other severe infections. [72] [73]

Do not use hypotonic crystalloids, starches or gelatins for resuscitation.

- Starches are associated with an increased risk of death and acute kidney injury compared with crystalloids. The effects of gelatins are less clear, but they are more expensive than crystalloids. [1] [75] Hypotonic (vs isotonic) solutions are less effective at increasing intravascular volume. *Surviving Sepsis* also suggests albumin for resuscitation when patients require substantial amounts of crystalloids, but this conditional recommendation is based on low-quality evidence. [1]

In adults, administer vasopressors when shock persists during or after fluid resuscitation. The blood pressure target should be MAP ≥ 60-65 mmHg in adults and improvement of markers of perfusion.

In children administer vasopressors if signs of fluid overload are apparent or the following persist after two fluid boluses:

- there are signs of shock such as altered mental state;
- tachycardia or bradycardia (HR < 90 bpm or > 160 bpm in infants and HR < 70 bpm or > 150 bpm in children);
- prolonged capillary refill (> 2 seconds) or feeble pulses;
- tachypnea; mottled cool skin or petechial or purpuric rash; increased lactate; persisting oliguria; or
- age-appropriate blood pressure targets are not achieved

If central venous catheters are not available, vasopressors can be given through a peripheral IV, but use a large vein and monitor closely for signs of extravasation and local tissue necrosis. If extravasation occurs, stop the infusion and consider local injection of phentolamine. Vasopressors can also be administered through intraosseous needles.

If signs of poor perfusion and cardiac dysfunction persist despite achieving the MAP target with fluids and vasopressors, consider an inotrope such as dobutamine.

- Vasopressors (i.e. norepinephrine, epinephrine, vasopressin, and dopamine) are most safely given through a central venous catheter at a strictly controlled rate, but it is also possible to administer them safely via peripheral vein and intraosseous needle. [76] Monitor blood pressure frequently and titrate the vasopressor to the minimum dose necessary to maintain perfusion and prevent side effects.
- Norepinephrine is considered first-line in adult patients; epinephrine or vasopressin can be added to achieve the MAP target. Because of the risk of tachyarrhythmia, reserve dopamine for selected patients with low risk of tachyarrhythmia or those with bradycardia.
- In children, epinephrine is considered first-line treatment, while norepinephrine can be added if shock persists despite optimal dose of epinephrine.

- No RCTs have compared dobutamine with placebo for clinical outcomes
- See Section 10.0 for remarks on corticosteroids and sepsis.

8.3 Prevention of Complications

Implement the interventions shown in Table 2 below to prevent complications associated with critical illness. These interventions are based on *Surviving Sepsis* and other guidelines and are considered to be feasible and based on high quality evidence. [1] [77] [78] [79] [80]

Careful consideration should be given to the numerous, clinically significant side-effects of medications that may be used in the context of COVID-19, as well as drug-drug interactions between medications, both of which may affect COVID-19 symptomatology (including effects on respiratory, cardiac, immune and mental and neurological function). Both pharmacokinetic and pharmacodynamic effects should be considered.

TABLE 2 – PREVENTION OF COMPLICATIONS IN CRITICALLY ILL PATIENTS

Anticipated outcome	Interventions
Reduce days of invasive mechanical ventilation	• Use weaning protocols that include daily assessment for readiness to breathe spontaneously; • Minimize continuous or intermittent sedation, targeting specific titration endpoints (sedation score targeted light sedation unless contraindicated) or with daily interruption of continuous sedative infusions; • Early mobilization; • Implementation of the above as a bundle of care (such as the Awakening and Breathing Coordination, Delirium assessment/management, and Early mobility [ABCDE]) may also reduce delirium.
Reduce incidence of ventilator-associated pneumonia	• Oral intubation is preferable to nasal intubation in adolescents and adults; • Keep patient in semi-recumbent position (head of bed elevation at 30–45^{o}); • Use a closed suctioning system; periodically drain and discard condensate in tubing; • Continue regular oral care • Use a new ventilator circuit for each patient; once patient is ventilated, change circuit if it is soiled or damaged, but not routinely; • Change heat moisture exchanger when it malfunctions, when soiled, or every 5–7 days.
Reduce incidence of venous thromboembolism	• Use pharmacological prophylaxis (low molecular-weight heparin [preferred] or heparin subcutaneously twice daily) in children, adolescents and adults without contraindications, and based on an assessment of individual risk factors for both thrombosis and bleeding. For those with contraindications, use mechanical prophylaxis (intermittent pneumatic compression devices).
Reduce incidence of catheter-related bloodstream infection	• Use a checklist with completion verified by a real-time observer as a reminder of each step needed for sterile insertion and as a daily reminder to remove catheter if no longer needed.

Anticipated outcome	Interventions
Reduce incidence of pressure ulcers	• Turn patient every 2 hours.
Reduce incidence of stress ulcers and gastrointestinal bleeding	• Give early enteral nutrition (within 24–48 hours of admission); • Consider administering histamine-2 receptor blockers or proton-pump inhibitors in patients with risk factors for GI bleeding. Risk factors for gastrointestinal bleeding include mechanical ventilation for ≥ 48 hours, coagulopathy, renal replacement therapy, liver disease, multiple comorbidities, and higher organ failure score. Stress ulcer prophylaxis should be reassessed as the patient's condition improves and as enteral feeding is established.
Reduce incidence of ICU-related weakness	• Actively mobilize the patient early in the course of illness when safe to do so.
Reduce the development of antimicrobial resistance	• Utilize de-escalation protocols as soon as patient is clinically stable and there is no evidence of bacterial infection.
Promote appropriate antimicrobial prescribing and use during the COVID- 19 pandemic	• Do not prescribe antibiotics to suspected or confirmed COVID-19 patients with low suspicion of a bacterial infection, to avoid short-term side- effects of antibiotics and negative long-term consequences of increased antimicrobial resistance.

9.0 Special Considerations

9.1 Caring for Pregnant Women with COVID-19

The Society for Obstetrician and Gynecologists Canada (SOGC) has published COVID-19 resources on obstetric and perinatal care to assist obstetricians in Canada. These resources can be found on their website at https://sogc.org/. To date, there are limited data on clinical presentation and perinatal outcomes after COVID-19 during pregnancy or the post-partum period. There is no solid evidence that pregnant women present with different signs or symptoms or are at higher risk of severe illness. The literature is mixed regarding whether pregnant women are at higher risk of severe illness, however it appears that the rates are not significantly higher, with reports of 4% or women requiring ICU admission and 3% requiring mechanical ventilation, which are similar to the non-pregnant population.

The section below on COVID-19 and pregnancy builds on existing recommendations and provides additional remarks for the management of pregnant and recently pregnant women.

Pregnant and recently pregnant women with suspected or confirmed COVID-19 should be isolated and treated with the supportive and management therapies previously described for other adults, taking into account the immunologic and physiologic adaptations occurring during and after pregnancy.

- Evidence of increased adverse maternal or neonatal outcomes is uncertain. Some literature has reported higher rates of stillbirth and many reports suggest higher rates of preterm birth but recent (August 5, 2020

- Living Systematic Reviews from the WHO collaborating centre for global women's health COVID-19 in Pregnancy (PregCOV-19LSR)), found a cumulative rate of preterm birth in 14,210 women from 49 cohort studies of 17%. In addition, there are reports of higher rates of fetal distress in labour particularly associated with maternal infection in the third trimester. (https://www.birmingham.ac.uk/research/who-collaborating-centre/pregcov/about/baby-outcomes.aspx) [81] [82]. Until more evidence becomes available, pregnant women with COVID-19 need to be observed closely for severe illness.

Pregnant women with a suspected, probable or confirmed COVID-19 infection, including women who may need to spend time in isolation, should have access to woman-centred, respectful skilled care, including obstetric, foetal medicine and neonatal care, as well as mental health and psychosocial support, with readiness to care for maternal and neonatal complications.

- Prevention of complications as described earlier, also apply to pregnant and recently pregnant women including those with miscarriage, late pregnancy fetal loss and postpartum/post-abortion women.
- The mode of delivery should be individualized based on obstetric indications.
- Multidisciplinary consultations from obstetric, perinatal, neonatal, infectious disease and intensive care specialists should be provided as required.
- Access to reproductive health care including termination of pregnancy should be ensured throughout the pandemic.

All recently pregnant women with COVID-19 infection or who have recovered from COVID-19 should be provided with counselling on safe infant feeding, including recommendations for breast feeding and appropriate infection prevention measures to prevent COVID-19 transmission (see section 9.2 below).

Pregnant and recently pregnant women who have recovered from COVID-19 should be encouraged to attend enhanced antenatal, postpartum or other obstetrical care as appropriate. Enhanced fetal surveillance is recommended for women with COVID-19 illness.

9.2 Caring for Infants and Mothers with COVID-19 – IPC and Breastfeeding

Relatively few cases have been reported of infants confirmed with COVID-19 infection. At this time there is no clear evidence that vertical transmission occurs. Breast milk samples from the mothers after the first lactation were negative for SARS CoV-2. [81] [82] Although recommendations for infant feeding varies around the world, Canadian recommendations are found below. Additional guidance on feeding and caring for infants and young children of mothers with COVID-19 is available on the WHO website:
https://www.who.int/publications/i/item/clinical-management-of-covid-19

Infants born to mothers with suspected, probable, or confirmed COVID-19 should be fed according to standard infant feeding guidelines, primarily breast feeding while providing necessary infection prevention precautions.

Symptomatic mothers who are breastfeeding should practice respiratory hygiene, including during feeding (for example, use of a mask when near a child if the mother has respiratory symptoms), perform hand hygiene before and after contact with the child, and routinely clean and disinfect surfaces with which the symptomatic mother has been in contact.

In situations when severe illness in a mother due to COVID-19 or other complications prevents her from caring for her infant or prevents her from continuing direct breastfeeding, mothers should be encouraged

and supported to express milk, and safely provide breast milk to the infant, while applying appropriate IPC measures.

Mothers and infants should be allowed to remain together and to practice rooming-in if desired, especially during establishment of breastfeeding, whether they or their infants have suspected, probable or confirmed COVID-19.

Parents and caregivers who may need to be separated from their children, and children who may need to be separated from their primary caregivers, should have access to appropriately trained health or non-health workers for mental health and psychosocial support.

9.3 Caring for Older Persons with COVID-19

Older age and comorbid conditions such as diabetes and cardiovascular disease have been reported as risk factors for death in persons with COVID-19. [40] Because older persons are at highest risk for severe disease and fatality and are one of the most vulnerable populations, they should be screened for COVID-19 at the first point of access to the health system, be diagnosed promptly if they are suspected to have COVID-19 and treated appropriately. As older patients may present with atypical symptoms, health workers should take this into account during the screening process.

- **Identify if there is an advance care plan for patients with COVID-19 and ensure the care plan takes into consideration their priorities and preferences. Tailor the care plan to be in line with the patient's expressed wishes (refer to section 9.5 for additional guidance on palliative care)**
- **For older persons with probable or suspected COVID-19, in addition to a conventional history the assessment should include an understanding of the person's life, values, priorities and preferences for health management.**
- **Ensure multidisciplinary collaboration (physicians, nurses, pharmacists and other health professionals) in the decision-making process to address multimorbidity and functional decline.**
- Physiological changes with age lead to declines in intrinsic capacity such as malnutrition, cognitive decline, depressive symptoms, and those conditions interact at several levels.
- Hearing and vision impairments become more prevalent among older adults and may pose a communication barrier, especially when masks prevent lip reading and decrease vocal clarity. Cognitive decline may also need to be considered when communicating with older patients.
- Older people who experience COVID-19, including those admitted to ICU and/or treated with protracted oxygen therapy and bed rest, are more likely to experience pronounced functional decline and may require coordinated rehabilitation care after acute hospitalization.

Early detection of inappropriate medication prescriptions is recommended to prevent adverse drug events and drug interactions in those being treated for COVID-19.

- Older patients are at greater risk of polypharmacy which increases the risk of negative health consequences. If medications are prescribed for mental and neurological manifestations of COVID-19 in older adults, this should be done with extreme caution given the increased susceptibility to drug side-effects and drug interactions with other prescribed medications.

Where appropriate, involve caregivers and family members in decision-making and goal setting throughout the management of older COVID-19 patients.

Symptom-based and palliative care should be provided, as appropriate, even for patients with supportive or curative goals of care.

9.4 Managing Patients with COVID-19 in Remote and Isolated Communities

While primary health care services are available in most remote and isolated communities, there is limited capacity to provide acute care and they may lack appropriate medical equipment, supplies and services (e.g., ventilators, access to specialists) to treat patients with severe illness. In many remote and isolated communities, a nurse-led health care team can provide emergency resuscitation and stabilization, emergency ambulatory care and outpatient non-urgent services. Access to physician services is available remotely via telehealth or teleconference, but much variation exists from community to community regarding the availability and frequency of physicians. Severely ill patients requiring complex emergency medical care are evacuated to a secondary or tertiary hospital or facility.

Treatment considerations for these remote and isolated settings include the following measures:

- Primary care providers or nursing stations, where available, should plan to provide triage and assessment, primary care treatment and monitoring.
- Mild disease, including uncomplicated pneumonia, should be managed within the community, with appropriate precautions in place.
- Alternate arrangements for self-isolation may be needed for persons in crowded living arrangements.
- Fluid management should be conservative when there is no evidence of shock, because aggressive fluid management may worsen oxygenation in settings without access to mechanical ventilation.
- Mild cases may progress to lower respiratory tract disease. Possible risk factors for progression to severe illness include older age and underlying chronic medical conditions such as lung disease, cancer, heart failure, cerebrovascular disease, renal disease, liver disease, diabetes, immunocompromising conditions, and pregnancy. [28] [83]
- Patients should be carefully monitored for signs of impending deterioration so that transfer can be arranged before intubation is required. Clinicians should be aware of the potential for some patients to rapidly deteriorate 1 week after illness
- Anticipate delays in accessing hospital care (awaiting air-ambulance, weather issues). Therefore, a low threshold should be considered for medevac options, particularly for the elderly, persons with underlying medical conditions or persons with evidence of pneumonia.

9.5 Palliative care and COVID-19

- **We recommend identifying, in all patients with COVID-19, if they have an advance care plan for COVID-19 (such as desires for intensive care support) and to discuss goals of care in the setting of acute illness. Patient priorities and preferences should be respected and their care plan tailored to allow the provision of the best care irrespective of treatment choice.**

- ☑ **Palliative care services should be made accessible at each institution that provides care for persons with COVID-19, and symptomatic treatments (e.g. management of dyspnea) should be provided even for patients with supportive or curative goals of care.**

9.6 Immunocompromised patients and COVID-19

- ☑ **Patients living with HIV Infection should be offered standard of care.**
  - Case series of patients living with HIV and COVID-19 have not shown a higher COVID-19 infection rate or complication rate in patients with suppressed viral loads and CD4> 200. It is assumed that patients with CD4<200 or not receiving Antiretroviral therapy will be at increased risk of disease due to their immunosuppression. [84]
- ☑ **In solid organ transplant patients, the risk of COVID 19 infection from a living donor or deceased donor is unknown at this time and such decisions on transplantation are to be made with expert advice.**
- ☑ **In Hematopoietic Stem Cell Transplantation (HSCT) patients, it is recommended that all recipients should have a negative COVID 19 PCR test prior to start of conditioning**
  - In HSCT patients, if a donor has travelled to a high risk area for COVID 19 transmission or has had contact with a patient confirmed to have COVID-19, the donor must be excluded from donation for at least 28 days.

10.0 Specific and Adjunctive COVID-19 Treatments and Clinical Research

There are many ongoing clinical trials testing various potential medical treatments. Until specific therapies become available, any medication should be given as part of a randomized controlled trial.

- ☑ **Collect standardized clinical data on all hospitalized patients to improve our understanding of the natural history of disease.**
- ☑ **Among hospitalized adult patients who have COVID-19 and require supplemental oxygen or mechanical ventilation, clinicians should strongly consider dexamethasone 6 mg IV daily for 10 days (or until discharge if earlier) or equivalent glucocorticoid dose.**
  - The recommendation is based on the data from a preliminary report of the RECOVERY trial comparing the use of 6 mg of dexamethasone given once daily for up to ten days. The primary outcome was 28-day mortality in more than 6,400 patients randomly allocated (1:2) to receive dexamethasone or usual care. [85]
  - While the trial demonstrated benefit of dexamethasone use in patients who required supplemental oxygen or mechanical ventilation, it did not reduce mortality in patients who did not require respiratory support at randomization (17.8% vs. 14%, RR 1.18 [95% CI 0.91 to 1.55]).
  - There are currently no data on the use of dexamethasone in children with severe disease who require supplemental oxygen or mechanical ventilation, hence clinical judgement should be applied if considering use.

- If oral, IV and/or inhaled steroids are indicated for non-COVID-19 reasons (e.g., asthma or COPD exacerbation, or stress dosing in someone on chronic steroids or with known adrenal insufficiency), they should not be avoided. [86] [87] [88] [89] [90] [91] [92] [93]

Consider the use of Remdesivir, either as a therapy or preferably as part of a randomized controlled trial.

- Data from a preliminary report of a multinational, randomized, placebo-controlled trial (the Adaptive COVID-19 Treatment Trial [ACTT]) of hospitalized patients with severe disease who received Remdesivir showed a shorter median time to clinical recovery compared to patients who received placebo (11 vs 15 days; rate ratio for recovery 1.32 [95% CI 1.12 to 1.55]). [94] The benefit of Remdesivir on reducing time to recovery was highest among patients who were not intubated but required supplemental oxygen. In mechanically ventilated patients who received Remdesivir there was no observed decrease in time to recovery. [95] Health Canada has authorized the use of Remdesivir for adults and adolescents aged 12 and over, and clinical trials are presently underway in children.

Do not use hydroxychloroquine or ritonavir/lopinavir outside of a clinical trial.

- The use of hydroxychloroquine and lopinavir-ritonavir in COVID-19 patients was recently reported in a large randomized, controlled, open-label, adaptive, platform trial (the RECOVERY trial). In the hydroxychloroquine arm of the trial, patients were randomised to receive either hydroxychloroquine (n=1,561) or usual care (n=3,155). [96] There was no significant difference in the primary endpoint of 28-day mortality or beneficial effects on hospital stay duration. In the lopinavir-ritonavir arm of the trial, patients were randomised to receive lopinavir-ritonavir (n=1,596) or usual care (n=3,376). [97] There was no significant difference in the primary endpoint of 28-day mortality, the risk of progression to mechanical ventilation or length of hospital stay. Based on these results, the use of hydroxychloroquine and lopinavir-ritonavir in COVID-19 patients should not be considered outside of a clinical trial setting.

Use of investigational anti-COVID-19 therapeutics should be done under ethically approved, randomized, controlled trials.

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