Orientation Manual to COVID Medicine at Sunnybrook Health Sciences Centre

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Section 1: Clinical Pearls

1.1 Clinical features/presentation (data predates the Omicron variant)

· Typical symptoms:

- Fever (can be ongoing/persistent), cough (dry or productive), sore throat, rhinorrhea, shortness of breath, muscle aches, fatigue (can be profound), headache

· Less common symptoms:

- Nausea, vomiting, diarrhea (~20% have GI symptoms)
- Neurological complications (stroke, decreased level of consciousness, muscle injury)
    - The elderly may present only with delirium
- Skin manifestations: Maculopapular, urticarial, and vesicular exanthems; transient livedo reticularis; “COVID toes” (Reddish-purple nodules on the distal digits similar in appearance to chilblains)

*Anosmia and dysgeusia may be early symptoms of COVID and should be included in review of systems

*Consider exacerbation of pre-existing condition as COVID presentation:

- Heart failure, atrial fibrillation, coronary artery disease, COPD, etc.

· Most common lab findings:

- Lymphopenia, elevated D-dimer, elevated LDH, elevated CRP
    - Lymphopenia associated with worse prognosis
    - Unclear value in ordering routine D-dimers or LDH

· Other lab findings:

- Mild elevation in AST/ALT, CK
- Thrombocytopenia, increased creatinine, and increased troponin associated with worse prognosis

· Imaging findings:

- Chest X-ray is often suggestive of atypical or viral pneumonia. Infiltrates are commonly bilateral, multifocal, peripheral, and have basal predominant distribution
    - May be normal in 20% of COVID patients
- CT Chest may suggest COVID (ground-glass opacities, crazy paving, consolidation, bronchovascular thickening, traction bronchiectasis). Routine CT Chest is not recommended due to lack of impact on management

*Note about tests:

- Each test ordered (bloodwork, radiology, etc) puts individuals at risk of exposure
- Avoid tests that will not change management
    - E.g. ordering LDH or D-dimer to diagnose COVID
    - E.g. ordering routine CT chest on patient with confirmed or suspected COVID without another indication to do so (e.g. suspicion of PE)

1.2 Diagnosis

· Mid-Turbinate swab (MT swab):

- PCR highly specific for COVID, but lower sensitivity and negative predictive value (5-40% false negative rate)
    **Therefore, in patients with clinical presentations consistent with COVID or high-risk exposures, a negative swab should be interpreted with caution. A low threshold for retesting and maintaining droplet/contact precautions is recommended. These decisions are guided by Infection Prevention and Control (IPAC), who are responsible for the decision to discontinue precautions*

· Samples from lower respiratory tract (endotracheal aspirate or expectorated sputum):

- May have higher sensitivity than MT/NP swab
- Bronchoscopy has highest yield
    - Given risk of exposure and transmission with aerosolizing procedures, bronchoscopy is not performed for COVID diagnosis (except, rarely, in intubated patients). In cases of diagnostic uncertainty, serial testing of upper respiratory tract specimens is preferred.

· Alternate diagnoses:

- Consider alternate or concomitant diagnoses (e.g. heart failure, bacterial sepsis, VTE, and other usual conditions)

1.3 Clinical course (pre-Omicron variant)

· Symptoms:

- Typical onset is 4-5 days after exposure; can appear up to 14 days after exposure
- Fever may persist for 4-12 days or even longer
- Course may be biphasic—patient may feel like they are improving after one week and then worsen thereafter in the second week
- Shortness of breath (when present) occurs at a median of 5 days (between days 5-12)
    - For those who develop respiratory decompensation beyond day 12, consider alternative diagnosis (bacterial super-infection, VTE)
        - However, patients with Variants of Concern sometimes develop respiratory decompensation beyond 12 days after symptom onset

- Cough lasts median of 19 days

· Severity:
- ~80% have mild to moderate symptoms
- ~15% have severe symptoms (hypoxemia or >50% lung involvement)
- ~5% have critical symptoms (respiratory failure, shock, multiorgan dysfunction)

· Timing of complications from symptom onset:

*Highest risk period for decompensation is days 8-12 after symptom onset
- When they arise as complications, sepsis, ARDS, ACS, arrhythmias, and Guillain-Barré syndrome typically occur during the second week after symptom onset
- Highest risk of AKI and secondary infection is during the third week after symptom onset
- Highest risk of VTE ~3-18 days after day of admission
- Multisystem Inflammatory Syndrome (~4 weeks after symptom onset, more common in children/adolescents, similar to Kawasaki/toxic shock syndrome, with persistent fever, multi-organ involvement, elevated inflammatory markers)

· Factors associated with poor prognosis:
- Increased age
- Male sex, non-Caucasian ethnicity (Black, Hispanic)
- Comorbidities: heart disease, diabetes, hypertension, chronic lung disease, chronic kidney disease, obesity, smoking, and cancer)
- Lab values: Lymphopenia, thrombocytopenia, elevated creatinine, elevated D-dimer

1.4 Oxygen Management

· Considerations:
- Severe hypoxia may not be accompanied by shortness of breath or increased work of breathing
- Oxygen flow > 6L by nasal prongs may spread droplets a greater distance
- Oxygen via face mask using a HEPA filter (Hi-OX mask is used at Sunnybrook) may decrease spread of droplets within patient's room
- Consider involving Rapid Response for any such patient desaturating on Venturi mask

· Respiratory escalation algorithm:
- Target SpO_2 > 90% in most patients
    - Avoid hyperoxia—do not target >95%
    - 88 – 92% target in chronic CO_2-retaining patients
- If hypoxic, can titrate nasal prongs up to 6L
- If hypoxic on 5-6L by NP, switch to oxygen via face mask using a HEPA filter

- If hypoxic on face mask: with the help of RT and Rapid Response, determine whether the patient requires admission to the ICU and/or initiation of high flow nasal cannula (HFNC)

1.5 Treatment

See Ontario Science Table recommendations:
https://covid19-sciencetable.ca/sciencebrief/clinical-practice-guideline-summary-recommended-drugs-and-biologics-in-adult-patients-with-covid-19-version-7-0/

· Dexamethasone:

- 6 mg PO/IV daily x10 days or until discharge if sooner
- Indication: any patient with COVID who has an O2 saturation measured at rest on room air that is < 92%
    - Reduced overall mortality by 17% in patients with COVID-19 (benefit seen in subgroups who are on supplemental O2, and those in ICU with invasive or non-invasive ventilation (RECOVERY Trial, NEJM, July 2020)
- No role in patients who do not require oxygen (non-significant trend towards higher mortality in this subgroup)
- Monitor for hypertension, hyperglycemia (e.g. consider ordering POCT blood glucose), and other side effects of corticosteroids

Strongyloides Screening and Pre-Emptive Therapy in Patients Receiving Dexamethasone for COVID

1. Screen all patients admitted with COVID-19 for epidemiological risk of Strongyloides hyperinfection within 24 hours of admission or 24 hours of diagnosis for nosocomial COVID infection.
2. Determine epidemiological risk (as per CATMAT guidelines):

Patients who were born in, resided in, or have long-term travel (cumulative 6-months exposure) to the following:

High Risk	Moderate Risk	Low Risk
• Southeast Asia • Oceania • Sub-Saharan Africa • South America • Caribbean	• Mediterranean • Middle East • North Africa • Indian sub-continent • Asia	• North America • Western Europe • Eastern Europe • Australia

3. Order Strongyloides serology in all moderate and high risk patients on admission.
4. We are no longer giving ivermectin prophylaxis in moderate and high risk groups.
5. Consult Infectious Diseases immediately if serology is positive or the patient develops a symptomatic Strongyloides infection.

· Tocilizumab:

- In REMAP trial, among 353 patients requiring high flow nasal oxygen, non-invasive positive pressure ventilation, or intubation, Tocilizumab reduced hospital mortality by 7.8%

- Side effects include infusion reactions, increase in AST/ALT, hypercholesterolemia, neutropenia, thrombocytopenia, diarrhea, and reactivation of latent infections like Hepatitis B or Strongyloides (therefore, recommend screening for Hepatitis B with HBsAg in all and Strongyloides in at-risk patients)

INFECTION SCREENING:

- Screen for Hepatitis B (with Hepatitis B surface antigen) in all patients
- Screen for Strongyloides in at-risk patients

CRITERIA FOR USE:

- Mildly Ill (i.e. non-hospitalized patients, hospitalized patients who do not require supplemental oxygen): Tocilizumab is not recommended outside of clinical trials for patients who are mildly ill with suspected or confirmed COVID-19.
- Moderately Ill (i.e. hospitalized patients requiring low-flow supplemental oxygen): Tocilizumab is recommended for patients who are moderately ill with suspected or confirmed COVID-19, who:
  - have evidence of systemic inflammation, defined as a CRP 75 mg/L or higher; AND
  - have evidence of disease progression (i.e., increasing oxygen or ventilatory requirements) despite 24-48 hours of optimal dexamethasone therapy;
  - AND are within 14 days of hospital admission (or within 14 days of a new COVID-19 diagnosis if nosocomially acquired).
- Critically Ill (i.e. hospitalized patients requiring oxygen by high flow nasal cannula, non-invasive ventilation, invasive mechanical ventilation): Tocilizumab is recommended for patients who are critically ill with suspected or confirmed COVID-19 who:
  - are on optimal dexamethasone therapy; AND
  - are within 14 days of hospital admission (or within 14 days of a new COVID-19 diagnosis if nosocomially acquired).

EXCLUSION CRITERIA:

- Known hypersensitivity to tocilizumab
- ANC < 2 $x10^9$/L
- PLT < 50 $x10^9$/L
- AST/ALT > 5X ULN

DOSE:

- 400 mg IV x1
- ID approval is required for administration

· Baricitinib:

- If the patient meets criteria to be given Tocilizumab but Tocilizumab is unavailable, recommend using Baricitinib instead
- Dose is 4 mg PO/NG daily x14 days or until hospital discharge
- Adverse effects include AST/ALT elevations, DVT/PE, thrombocythemia, and increased CK
- ID approval is required for administration

· Remdesivir:

- Indicated in moderately ill patients (those requiring oxygen but not requiring mechanical ventilation)
- Dose: 200 mg IV on Day 1, then 100 mg IV daily x4 more days
- Side effects include nausea, vomiting, bradycardia, and increase in liver enzymes
- Order baseline liver enzymes prior to initiation, and then on days 3 and 5 of therapy
- Discontinue remdesivir if ALT or AST ≥ 5X ULN

· Other therapies:

- Consider empiric therapy with Ceftriaxone 1g IV q24h x5 days only if bacterial co-infection/superinfection is strongly suspected
    - Bacterial co-infection has been found to be quite rare—~8%
- Azithromycin only if concern for Legionella infection

** Hydroxychloroquine, Lopinavir/ritonavir, Ivermectin, and routine antibiotics have been found to be of no clinical benefit and are not recommended*

· Intravenous fluids:

- Fluid-restrictive resuscitation
    - Patients with COVID may develop ARDS and may be at a higher risk of pulmonary edema
    - Avoid continuous IV fluids if patient is clinically euvolemic unless patient is NPO

1.6 Anticoagulants

· Anticoagulant considerations:

- VTE prophylaxis is given at intermediate doses for patients with COVID:
    - If CrCl > 30 mL/min:
        - If weight < 50 kg – Use Enoxaparin 30 mg SC bid
        - If weight between 50-100 kg – Use Enoxaparin 40 mg SC bid
        - If weight > 100 kg – Use Enoxaparin 60 mg SC bid
    - If CrCl 10-30 mL/min:
        - If weight 60-110 kg – Use Tinzaparin 8000 units SC qHS
        - If weight < 60 kg or > 110 kg, page Thromboembolism team
    - If high risk for bleed – Use bilateral below-knee TED stockings

- Pulmonary embolism: Consider PE as a potential cause for clinical decompensation
- DOACs: Direct oral anticoagulants (DOACs) may have clinically important drug-drug interactions with both typical and investigational treatments (please review with pharmacy)

1.7 Treatment of the Mildly Ill

· Defined as those with COVID who do not need supplemental oxygen (or more than usual)

- Do not always require admission unless for another indication or are at very high risk of decompensation
    - Note that patients with mild COVID should not be admitted solely to administer COVID-specific IV medications outlined below; the IV medications may only be appropriate if admission is indicated for another reason or if administration is possible in their outpatient locale
- Should still be considered hypercoagulable and treated with intermediate dose VTE prophylaxis if inpatient

· Treatment of mildly ill patients depends on their risk of developing severe disease:

- Higher risk of severe disease defined as:
    - Immunocompromised, or
    - Unvaccinated patients (< 2 doses) with one or more of:
        - ≥ 60 years of age
        - Indigenous and ≥ 50 years of age
        - ≥ 50 years of age and ≥1 risk factors (CKD stage 5, diabetes, obesity, cerebral palsy, intellectual disability, sickle cell disease, cancer on active treatment, or solid organ transplant/stem cell transplant)
- Moderate risk of severe disease defined as:
    - Vaccinated ≥ 60 years of age
    - Vaccinated Indigenous and ≥ 50 years of age
    - Vaccinated ≥ 50 years of age and ≥1 risk factors (CKD stage 5, diabetes, obesity, cerebral palsy, intellectual disability, sickle cell disease, cancer on active treatment, or solid organ transplant/stem cell transplant)
- Lower risk of severe disease defined as:
    - Any patient not meeting above criteria

· Treatment of **higher risk** patients:

- Sotrovimab:
    - Indicated in this patient group if within 7 days of symptom onset
    - Dose: 500 mg IV x1
- Remdesivir:
    - Only if Sotrovimab is unavailable and within 7 days of symptom onset
    - Dose in this population is 200 mg IV x1 then 100 mg IV daily x2 days
    - Side effects include nausea, vomiting, bradycardia, and increase in liver enzymes
    - Check liver enzymes at baseline and after treatment
- Fluvoxamine:
    - Only if Sotrovimab and Remdesivir are unavailable and within 7 days of symptom onset
    - Dose: 50 mg PO daily titrated up to 100 mg PO tid x 15 days

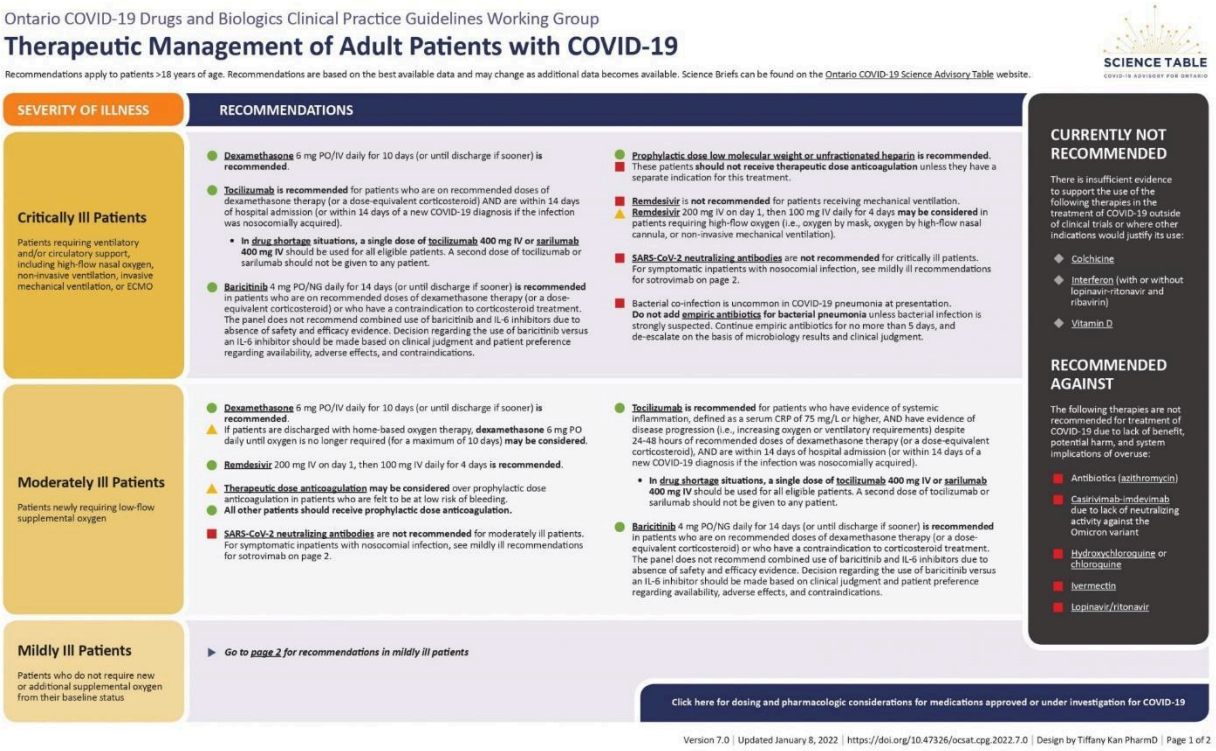
    - Drug interactions: Caution that Fluvoxamine is a cytochrome P450 (CYP450) inhibitor. Co-administration with a variety of drugs (see non-exhaustive list below) can result in clinically relevant drug-drug interactions. A medication review and consultation with a pharmacist is recommended
        - Potent inhibitor: CYP1A2 (e.g. clozapine, theophylline), CYP2C19 (e.g. clopidogrel, amitriptyline, PPIs)
        - Moderate inhibitor: CYP2C9 (e.g. warfarin, sulfonylureas), CYP3A4 (e.g. diazepam, atorvastatin, DOACs, etc.)
        - Mild inhibitor: CYP2D6 (e.g. codeine, tamoxifen, several beta-blockers, several SSRIs/SNRIs).
    - Serotonin syndrome: Caution that co-adminstration with other SSRIs/SNRIs or other pro-serotonergic drugs could precipitate serotonin syndrome
- Budesonide:
    - Mainly useful for reduction in duration of symptoms. Can be used in combination with the above therapies
    - Dose: 800 mcg inh bid x up to 14 days

· Treatment of **moderate risk** patients:

- Remdesivir as above
- Fluvoxamine as above if Remdesivir unavailable or contraindicated and the risk-benefit ratio warrants its use
- Budesonide for symptom reduction as above

· Treatment of **lower risk** patients:

- Reassurance and monitoring only; the above therapies are not recommended for this group.



Ontario COVID-19 Drugs and Biologics Clinical Practice Guidelines Working Group

Therapeutic Management of Adult Patients with COVID-19

Recommendations apply to patients >18 years of age. Recommendations are based on the best available data and may change as additional data becomes available. Science Briefs can be found on the Ontario COVID-19 Science Advisory Table website.

SCIENCE TABLE
COVID-19 ADVISORY FOR ONTARIO

SEVERITY OF ILLNESS	RECOMMENDATIONS
Critically Ill Patients Patients requiring ventilatory and/or circulatory support, including high-flow nasal oxygen, non-invasive ventilation, invasive mechanical ventilation, or ECMO	● **Dexamethasone** 6 mg PO/IV daily for 10 days (or until discharge if sooner) **is recommended**. ● **Tocilizumab** **is recommended** for patients who are on recommended doses of dexamethasone therapy (or a dose-equivalent corticosteroid) AND are within 14 days of hospital admission (or within 14 days of a new COVID-19 diagnosis if the infection was nosocomially acquired). • **In drug shortage situations, a single dose of tocilizumab 400 mg IV or sarilumab 400 mg IV** should be used for all eligible patients. A second dose of tocilizumab or sarilumab should not be given to any patient. ● **Baricitinib** 4 mg PO/NG daily for 14 days (or until discharge if sooner) **is recommended** in patients who are on recommended doses of dexamethasone therapy (or a dose-equivalent corticosteroid) or who have a contraindication to corticosteroid treatment. The panel does not recommend combined use of baricitinib and IL-6 inhibitors due to absence of safety and efficacy evidence. Decision regarding the use of baricitinib versus an IL-6 inhibitor should be made based on clinical judgment and patient preference regarding availability, adverse effects, and contraindications. ● **Prophylactic dose low molecular weight or unfractionated heparin** **is recommended**. ■ These patients **should not receive therapeutic dose anticoagulation** unless they have a separate indication for this treatment. ■ **Remdesivir** is **not recommended** for patients receiving mechanical ventilation. ▲ **Remdesivir** 200 mg IV on day 1, then 100 mg IV daily for 4 days **may be considered** in patients requiring high-flow oxygen (i.e., oxygen by mask, oxygen by high-flow nasal cannula, or non-invasive mechanical ventilation). ■ **SARS-CoV-2 neutralizing antibodies** are **not recommended** for critically ill patients. For symptomatic inpatients with nosocomial infection, see mildly ill recommendations for sotrovimab on page 2. ■ Bacterial co-infection is uncommon in COVID-19 pneumonia at presentation. **Do not add empiric antibiotics for bacterial pneumonia** unless bacterial infection is strongly suspected. Continue empiric antibiotics for no more than 5 days, and de-escalate on the basis of microbiology results and clinical judgment.
Moderately Ill Patients Patients newly requiring low-flow supplemental oxygen	● **Dexamethasone** 6 mg PO/IV daily for 10 days (or until discharge if sooner) **is recommended**. ▲ If patients are discharged with home-based oxygen therapy, **dexamethasone** 6 mg PO daily until oxygen is no longer required (for a maximum of 10 days) **may be considered**. ● **Remdesivir** 200 mg IV on day 1, then 100 mg IV daily for 4 days **is recommended**. ▲ **Therapeutic dose anticoagulation** **may be considered** over prophylactic dose anticoagulation in patients who are felt to be at low risk of bleeding. ● **All other patients should receive prophylactic dose anticoagulation.** ■ **SARS-CoV-2 neutralizing antibodies** are **not recommended** for moderately ill patients. For symptomatic inpatients with nosocomial infection, see mildly ill recommendations for sotrovimab on page 2. ● **Tocilizumab** **is recommended** for patients who have evidence of systemic inflammation, defined as a serum CRP of 75 mg/L or higher, AND have evidence of disease progression (i.e., increasing oxygen or ventilatory requirements) despite 24-48 hours of recommended doses of dexamethasone therapy (or a dose-equivalent corticosteroid), AND are within 14 days of hospital admission (or within 14 days of a new COVID-19 diagnosis if the infection was nosocomially acquired). • **In drug shortage situations, a single dose of tocilizumab 400 mg IV or sarilumab 400 mg IV** should be used for all eligible patients. A second dose of tocilizumab or sarilumab should not be given to any patient. ● **Baricitinib** 4 mg PO/NG daily for 14 days (or until discharge if sooner) **is recommended** in patients who are on recommended doses of dexamethasone therapy (or a dose-equivalent corticosteroid) or who have a contraindication to corticosteroid treatment. The panel does not recommend combined use of baricitinib and IL-6 inhibitors due to absence of safety and efficacy evidence. Decision regarding the use of baricitinib versus an IL-6 inhibitor should be made based on clinical judgment and patient preference regarding availability, adverse effects, and contraindications.
Mildly Ill Patients Patients who do not require new or additional supplemental oxygen from their baseline status	▶ *Go to page 2 for recommendations in mildly ill patients*

CURRENTLY NOT RECOMMENDED

There is insufficient evidence to support the use of the following therapies in the treatment of COVID-19 outside of clinical trials or where other indications would justify its use:

- ◆ Colchicine
- ◆ Interferon (with or without lopinavir-ritonavir and ribavirin)
- ◆ Vitamin D

RECOMMENDED AGAINST

The following therapies are not recommended for treatment of COVID-19 due to lack of benefit, potential harm, and system implications of overuse:

- ■ Antibiotics (azithromycin)
- ■ Casirivimab-imdevimab due to lack of neutralizing activity against the Omicron variant
- ■ Hydroxychloroquine or chloroquine
- ■ Ivermectin
- ■ Lopinavir/ritonavir

Click here for dosing and pharmacologic considerations for medications approved or under investigation for COVID-19

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Mildly Ill Patients

Patients who do not require new or additional supplemental oxygen from their baseline status

Tier 1

Immunocompromised individuals[1] not expected to mount an adequate immune response to COVID-19 vaccination or SARS-CoV-2 infection due to their underlying conditions, regardless of vaccine status; OR Unvaccinated[2] individuals at highest risk of severe disease (only if also age ≥70 years, Indigenous and age ≥60 years, or age ≥60 years with one or more risk factors[3]). Older immunocompromised individuals are at higher risk, and should be prioritized for treatment in this tier.[4]

Tier 2

Unvaccinated[2] individuals at risk of severe disease (only if also age ≥60 years, Indigenous and age ≥50 years, or ≥50 years with one or more risk factors[3]).[4]

Tier 3

Vaccinated individuals at highest risk of severe disease (only if also age ≥70 years, Indigenous and age ≥60 years, or age ≥60 years with one or more risk factors[3]). Vaccinated individuals who are >6 months from their last dose of vaccine are at higher risk, and should be prioritized for treatment in this tier.[4]

Tier 4

Vaccinated individuals at risk of severe disease (only if also age ≥60 years, Indigenous and age ≥50 years, or ≥50 years with one or more risk factors[3]). Vaccinated individuals who are >6 months from their last dose of vaccine are at higher risk, and should be prioritized for treatment in this tier.[4]

This guidance applies to mildly ill patients in any setting, including the community, hospital (including nosocomial cases), and congregate care settings.

● It is **recommended** that eligibility for outpatient therapies include patients who test positive for SARS-CoV-2 on either PCR or a healthcare-professional administered RAT or ID Now.

RISK LEVEL	RECOMMENDATIONS
HIGHER RISK OF SEVERE DISEASE Tier 1 Tier 2	● **Sotrovimab** 500 mg IV x 1 dose **is recommended** for these patients if they present within 7 days of symptom onset. • Previous SARS-CoV-2 infection and vaccination status do not need to be considered. Serologic testing is not recommended. • These individuals should have a reasonable expectation for 1-year survival prior to SARS-CoV-2 infection. • It is recommended that monoclonal antibody therapy be administered to non-hospitalized individuals across Ontario using a hybrid network that includes, but is not limited to, mobile integrated healthcare services, community paramedicine, and outpatient infusion clinics. *If sotrovimab is unavailable or contraindicated:* ▲ **Remdesivir** 200 mg IV on day 1, then 100 mg IV daily for 2 days **may be considered** for these patients if they present within 7 days of symptom onset and: (1) more effective therapeutic options (i.e. sotrovimab) are not available; and (2) intravenous administration is not a barrier. • These individuals should have a reasonable expectation for 1-year survival prior to SARS-CoV-2 infection. *If remdesivir is unavailable or contraindicated:* ▲ **Fluvoxamine** 50 mg PO daily titrated up to 100 mg PO TID for 15 days **may be considered** for these patients if they present within 7 days of symptom onset. This recommendation is based on very low certainty evidence of reduction in hospitalization, and the need for outpatient treatment options with a reasonable safety profile during an anticipated spike in COVID-19 cases due to the Omicron variant. Pharmacist consultation and outpatient provider follow-up is important to avoid any significant adverse drug interactions with fluvoxamine. ▲ **Budesonide** 800 mcg inhaled twice daily for 14 days **may be considered** for these patients. This recommendation is based on very low certainty evidence of reduction in duration of symptoms, and the need for outpatient treatment options with a reasonable safety profile during an anticipated spike in COVID-19 cases due to the Omicron variant. Budesonide may have a role as an additional therapy in patients already on other therapies who have respiratory symptoms.
MODERATE RISK Tier 3 Tier 4	▲ **Remdesivir** 200 mg IV on day 1, then 100 mg IV daily for 2 days **may be considered** for these patients if they present within 7 days of symptom onset and intravenous administration is not a barrier. • These individuals should have a reasonable expectation for 1-year survival prior to SARS-CoV-2 infection. *If remdesivir is unavailable or contraindicated:* ▲ **Fluvoxamine** 50 mg PO daily titrated up to 100 mg PO TID for 15 days **may be considered** for these patients if they present within 7 days of symptom onset. See fluvoxamine recommendation statement for higher risk mildly ill patients. ▲ **Budesonide** 800 mcg inhaled twice daily for 14 days **may be considered** for these patients. See budesonide recommendation statement for higher risk mildly ill patients. ■ **Sotrovimab** is **not recommended** for these patients. This recommendation is based on current limited supply of sotrovimab, and prioritizing its administration in patients at greatest risk of progressing to severe disease.
LOWER RISK *Any individual not included in tiers 1 to 4*	● **Reassurance and information for self-monitoring** of symptoms (including self-monitoring of oxygen saturation) **are recommended**. ■ **Sotrovimab** is **not recommended** for these patients. This recommendation is based on current limited supply of sotrovimab, and prioritizing its administration in patients at greatest risk of progressing to severe disease. ■ **Remdesivir** is **not recommended** for these patients. This recommendation is based on current limited supply of remdesivir, and prioritizing its administration in patients at greatest risk of progressing to severe disease (those who are moderately ill, followed by those who are mildly ill but at higher risk of progression). ■ **Fluvoxamine** is **not recommended**. ■ **Budesonide** is **not recommended**.

◆ There is currently **insufficient evidence** to make a recommendation around **aspirin** or **anticoagulation** for mildly ill patients.

■ The following therapies are **not recommended** in mildly ill patients: **dexamethasone**, **tocilizumab**, **sarilumab**, and **baricitinib**.

1. Examples of immunocompromised or immunosuppressed individuals include individuals with active treatment for solid tumor and hematologic malignancies, receipt of solid-organ transplant and taking immunosuppressive therapy, receipt of chimeric antigen receptor (CAR)-T-cell or hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy), moderate or severe primary immunodeficiency (e.g., DiGeorge syndrome, Wiskott-Aldrich syndrome, common variable immunodeficiency, Good's syndrome, hyper IgE syndrome), advanced or untreated HIV infection, active treatment with high-dose corticosteroids (i.e., ≥20 mg prednisone or equivalent per day when administered for ≥ 2weeks), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents classified as severely immunosuppressive, tumor necrosis factor (TNF) blockers, and other biologic agents that are immunosuppressive or immunomodulatory. For individuals who are immunosuppressed or receiving immunosuppressants, their condition is considered both an underlying risk factor AND a marker of insufficient ability to mount an immune response to SARS-CoV-2. These individuals should have a reasonable expectation for 1-year survival prior to SARS-CoV-2 infection.
2. Unvaccinated is defined as individuals who have received one or zero doses of a COVID-19 vaccine.
3. Risk factors include obesity (BMI ≥30), dialysis or stage 5 kidney disease (eGFR <15 mL/min/1.73 m²), diabetes, cerebral palsy, intellectual disability of any severity, sickle cell disease, receiving active cancer treatment, solid organ or stem cell transplant recipients. If patients have, in the opinion of a physician, other important risk factors for disease progression beyond this list that merit the use of specific drugs or therapeutics, these should be clearly documented at the time of administration.
4. Although pregnancy is a risk factor for severe COVID-19, the absolute risk for this population remains low due to the young age and lack of comorbidities of most pregnant individuals. Considerations for the use of specific COVID-19 therapeutics should therefore be made on a case-by-case basis.

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1.8 Discharge

· Discharge criteria (not a strict set of criteria):

- Clinically improving
- Not requiring supplemental oxygen
- Ability for self-care
    - Some rehab hospitals and other institutions may not accept while patient is still infectious. Others do accept infectious patients, so it is important to explore the possibility of discharge to these institutions

**Can self-isolate, or no longer requires self-isolation (see Isolation considerations below)*

· Oxygen considerations:

- If the patient still requires oxygen but is otherwise ready for discharge, the patient may qualify for home oxygen

· Isolation considerations:

- Public Health guidelines dictate that a COVID patient at home or returning home needs strict self-isolation until a minimum of 10 days following symptom onset (20 days following symptom onset in severe COVID requiring a stay in ICU or immunocompromised patient), at which point Public Health/IPAC may evaluate the need for further isolation
    - If patient is within the infectious window and is being discharged home, they may need to self-isolate until cleared by Public Health
        - They may be able to return home while infectious to live with household members they previously lived with if their household members are not high risk for complications
    - If patient is >10 days from symptom onset and cleared by IPAC, they can be discharged with “usual” social distancing practices (even if they are still having symptoms, as long as they are improving)

· Discharge process:

- Provide with info sheet on how to self-isolate (if necessary)
    - https://www.publichealthontario.ca/-/media/documents/ncov/factsheet-covid-19-how-to-self-isolate.pdf?la=en
- Patient should take private car home (taxi ok)
    - Best if patient drives themselves home
    - If being driven by someone else, patient should be only other person in the car, should sit in the back right, and the windows should be down if possible; driver and patient should both wear masks in the vehicle

1.9 Sources:

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Section 2: Personal Protective Equipment (PPE) Pearls

2.1 Preparation

· Before beginning to care for patients with suspected or confirmed COVID:
- Get access to hospital scrubs
    - Staff: email sally.ganesh@sunnybrook.ca
    - Residents: email sbdom.education@sunnybrook.ca
- Ensure your N95 mask fit testing is up to date
- Males to be clean-shaven (every day)
- Leave all jewelry and watches at home
- Review handwashing technique (https://tinyurl.com/uvj3fyr)
- Review proper donning and doffing of PPE (https://tinyurl.com/to8c7b3)
- Review proper donning and doffing of mask (https://tinyurl.com/vxdntyd)
- Get colleague to observe your donning and doffing of PPE and give feedback
- Clean your office surfaces with Cavi wipe or other cleaning method
- Leave your stethoscope behind
    - Not recommended to use either own or hospital stethoscope on patients with suspected or confirmed COVID, as stethoscope is easily contaminated
    - If critical to management, the floor may have disposable stethoscopes that can be used for this purpose

2.2 Daily routine

· Daily routine:
- See patients, write orders and notes, washing your hands any time you have just touched a surface, before you touch any object that should be clean, and in the usual donning and doffing moments of hand hygiene
    - Avoid touching your face!
- When possible, as you round, have your donning and doffing observed by a “buddy” or a ward safety monitor

2.3 Mask Pearls

· Key mask pearls while caring for patients with suspected or confirmed COVID:
- N95s are preferred over surgical masks when caring for patients with suspected or confirmed COVID

    - Mask with integrated visor should not be worn over an N95—if wearing an N95, use a face shield over it
- Can wear a face shield while going room to room on COVID ward without removing them
    - Can wear mask with integrated visor at nursing station, but remove face shield before coming to nursing station

Section 3: Management of pregnant inpatients with COVID-19

See Ontario Science table recommendations on the care of pregnant patients with COVID-19:
https://covid19-sciencetable.ca/sciencebrief/the-incidence-severity-and-management-of-covid-19-in-critically-ill-pregnant-individuals/

Services to involve

1) Internal medicine/COVID team
2) High risk-obstetrics; in particular for patients with a periviable gestation or later (>22w) in whom fetal monitoring is indicated
3) Clinical Pharmacology; for recommendations on safety of drugs in pregnancy
4) Infectious Diseases
5) Critical care

Initial investigations: Follow initial COVID investigations on the Sunnybrook order set.

Additional investigations to consider:

- - N95s are preferred over surgical masks when caring for patients with suspected or confirmed COVID
- If concerns about maternal cardiac involvement: BNP, d-dimer, troponin, ECG, and consider 2D echocardiogram (esp. if underlying cardiac disease)
- Pre-eclampsia: There is a higher risk of pre-eclampsia in patients with COVID-19. Close monitoring of blood pressure is necessary; HTN: >140/90; HTN requiring urgent intervention > 160/100.
    - Blood work: Urine PCR, uric acid, liver enzymes, CBC (r/o HELLP), and consider hemolysis work-up.
    - Blood pressure management: Suggest starting with labetalol (IV/PO) or nifedipine XL (other drugs: methyldopa, hydralazine).

Imaging (Obtain consent from the patient/SDM, provide shield for fetus)

- Investigations that are necessary for maternal care should be performed
- Chest CT (including CTPA) is appropriate in pregnancy when clinically indicated
- Generally accepted that up to 50 mGy is acceptable exposure in pregnancy
- Risk of oncogenicity associated with 150mGy fetal exposure
- Risk of teratogenicity associated with 100mGy fetal exposure

Very Low Dose (<0.1mGy)	
Chest X ray	0.0005-0.01
Head /Neck CT	0.001-0.01
Low-Moderate Dose (0.1-10 mGy)	

Abdominal X Ray	0.1-3
CT Chest/CT pulmonary angiography	0.01-0.66
Nuclear Medicine (Low Dose Perfusion Only)	0.02-0.2
Nuclear Medicine Ventilation Scan	0.1-0.3
High Dose 10-50mGy	
Abdominal /pelvic CT	1.3-35

Adapted from American College of Radiologists 2018

· Key mask pearls while caring for patients with suspected or confirmed COVID:
- N95s are preferred over surgical masks when caring for patients with suspected or confirmed COVID

Maternal Monitoring:

Vitals (Temperature, BP, HR, RR with O_2 saturation): q4h
Increase frequency of vitals q1-2h if:

- New use of oxygen support
- RR increases despite normal O_2 saturation
- Increasing amount of oxygen to maintain saturation >94%

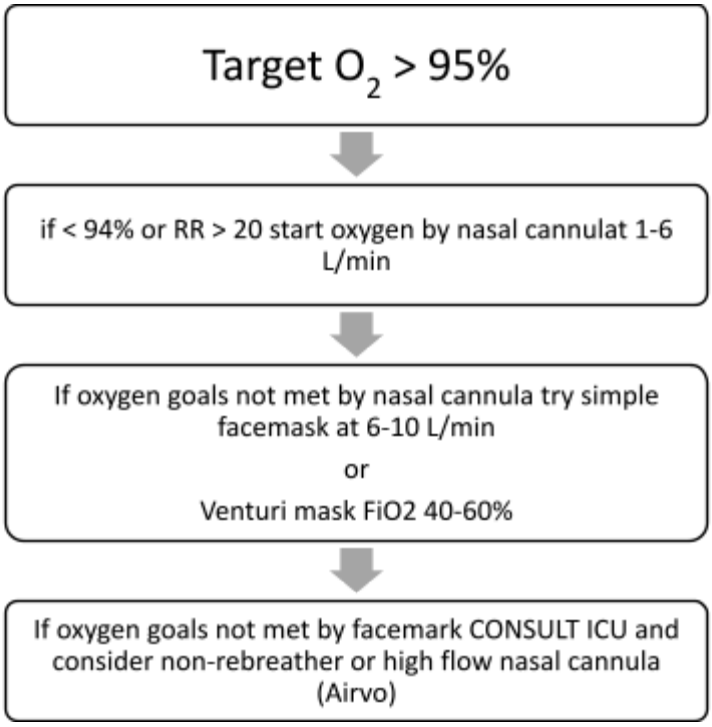
Abnormal vital signs differ in pregnant versus non-pregnancy individuals. The following vitals signs are abnormal in pregnant patients:
HR>115 or <60, RR>22 or <9, or SpO2<94%, or <96% with other abnormal vitals.

Warning signs of maternal deterioration: maternal vital sign changes precede acute maternal deterioration by 1-4h.*

- Increased O_2 demands by 50% over 1-2h
- O_2 sat < 94% despite O_2 support
- >4.0L O2 by facemask

* Indication to consult ICU team

Management of Oxygen Therapy:



COVID Pharmacotherapy:

Descriptions	Moderate Critical Illness	Severe Critical Illness	Refractory Hypoxia
Hypoxia Management	▪ Face mask oxygen ▪ High flow nasal cannula	▪ Intubations to be conducted by airway experts, if available, given unique obstetrical considerations ▪ Higher PEEP may be required ▪ Prone positioning ▪ Consider ECMO	▪ Consider ECMO
Drug Therapies	▪ Corticosteroids[a] ▪ Tocilizumab ▪ VTE prophylaxis ▪ Not recommended: Remdesivir if requiring high flow nasal cannula or non-invasive ventilation	▪ Corticosteroids[a] ▪ Tocilizumab ▪ VTE prophylaxis ▪ Not recommended: Remdesivir	▪ Corticosteroids[a] ▪ Tocilizumab ▪ VTE prophylaxis ▪ Not recommended: Remdesivir
Obstetrical Management	▪ Obstetrical and fetal assessment ▪ Consider corticosteroids for fetal lung maturation if indicated		
		▪ Discussions with OB, OB-anesthesia, NICU, critical care teams about indication, timing, whether delivery may be indicated based upon gestational age, fetal indications, impact of fetus on maternal physiology and severity of illness, whether an obstetrical indication exists	

Figure 2. COVID-19 Management Considerations in Pregnancy

Figure presenting a summary of available evidence for COVID-19 management in pregnancy. [a]Many institutions adopted the following approach to corticosteroids: If currently less than 22 or greater than 36 weeks gestation: methylprednisolone 32 mg IV x 1 dose, followed by methylprednisolone 32 mg IV (or prednisone 40 mg orally) daily for days 2-10. If currently 22 to 36 weeks gestation: dexamethasone 12 mg IV daily (or dexamethasone 6mg IV twice a day) for 2 days for fetal lung maturation followed by methylprednisolone 32 mg IV daily (or prednisone 40 mg orally daily) for days 3-10 (55). If post-partum (with or without breastfeeding) dexamethasone 6 mg orally or IV daily for 10 days or until hospital discharge. PEEP, positive end-expiratory pressure. ECMO, extracorporeal membrane oxygenation. OB, obstetrician or obstetrics. NICU, neonatal intensive care unit.

Remdesivir:

- Use same dosing as in non-pregnant patients: 200 mg IV on Day 1, 100 mg IV Days 2 – 5.
- Same exclusion criteria apply as in non-pregnant patients

Tocilizumab:

- Use same dose as in non-pregnant patients: 400 mg IV x1.
- The same criteria to use tocilizumab in non-pregnant patients should be applied to pregnant patients.

Thromboprophylaxis:

- Follow standard Sunnybrook DVT prophylaxis dosing for COVID patients

Antibiotic Therapy:

- Can call clinical pharmacology or ID service for specific questions regarding the safety of antimicrobials in pregnancy.

Other Therapies:

- Consult clinical pharmacology or ID service for consideration of other COVID-19 treatments (e.g. baricitinib, sotrovimab, fluvoxamine, budesonide, etc.)

Fetal considerations:

- High risk obstetrics should be involved early in the patient course due to the potential for rapid maternal decompensation. Neonatal resuscitation should be planned in the event of maternal decompensation (or need for urgent delivery) and obstetrics should consider involvement of the NICU team when appropriate.

- Fetal monitoring:
    - *Pre-viable gestational age*: Fetal heart rate daily
    - *Viable gestational age (> 25 w GA, 22-25w GA based on choice for neonatal resuscitation):* Daily NST with strict criteria for intervention: fetal tachycardia > 180 bpm not accounted for by maternal condition (tachycardia, fever), recurrent complex variable decelerations > 1hour, prolonged bradycardia. May consider FHR q4h with maternal vitals. Note: fetal heart rate changes may precede maternal deterioration and can be used as an adjunct to maternal surveillance.
    - Suggest baseline EFW and BPP (+/- Doppler study) to direct counselling regarding intervention for fetal indications.
    - After viability, for weekly BPP and q2weeks EFW
        - Anticipate abnormal BPP due to maternal sedation/heavy narcotics use
        - UA and DV Dopplers will help indicate fetal wellbeing
    - Continue monitoring fetal growth q2-4weeks post COVID recovery
    - If prolonged period of maternal hypoxemia, may consider fetal target neurosonogram and/or fetal brain MRI to evaluate for evidence of hypoxic-ischemic brain injury.
    - NO indication for continuous EFM

Considerations for Delivery

- COVID-19 infection is not an indication for delivery. Individualized decision taking into account maternal status, fetal status, gestational age and maternal wishes for fetal intervention
    - Delivery may trigger deterioration (via maternal autotransfusion increasing fluid load)
    - Delivery may be indicated in critically ill patients for maternal stabilization, and potentially improvement of respiratory status

Possible indications for delivery include intrauterine infection, DIC, hepatic/renal failure, compromised CV function thought to be due to gravid uterus, cardiac arrest, fetal demise

Worsening illness/ICU admission:

- Mechanical ventilation not indication for delivery if oxygenation can be maintained, important to balance risks of prematurity vs risks of HIE secondary to poor oxygenation
- Pre and periviable gestations: risk prematurity is great, do not deliver unless needed for maternal stabilization
- 25-32 weeks: individualized decision based on maternal and fetal status, parental wishes
- >32 weeks: consider delivery in cases of maternal hypoxic respiratory failure, need for ECMO
- After viability, consider keeping delivery tray at maternal bedside in case of rapid spontaneous onset of labour

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