This algorithm is meant to provide a framework for COVID-19 treatment decision making and is subject to change as more data becomes available.

**CLINICAL SIGNS/SYMPTOMS**
- Fever in >75% of hospitalized cases at some point.
  - Almost 50% are afebrile on admission
- Cough 60-80% dry/productive
- SOB 20-40%
- URI (HA, sore throat, rhinorrhea 4%)
- GI symptoms (diarrhea, nausea/vomiting) in <10%
  - Can be seen early on prior to respiratory symptoms
- Early symptoms: loss of taste and smell

**LABS AND BIOMARKERS**
- Median WBC 4.7, leukopenia in 30-45%
- Lymphopenia in 33-85%
- Median platelets normal but slight decrease in 35%
- AST/ALT increase in 4-22%
- CRP increase in 61-86%, ESR increase in up to 85%
- LDH increase in 27-75% Hgb decrease in 41-50%
- Albumin decrease in 50-98%
- Procalcitonin: ≥ 0.5 in 5% overall, (14% if severe, 24% if ICU)

**LABS**
- CBC with diff, CMP, procalcitonin, Ferritin, CPK, CRP, LDH, ESR, D-Dimer, +/- Troponin
- Look for: leukopenia, lymphopenia and transaminitis

**MICROBIOLOGY**
- Check Flu/RSV, Respiratory viral panel if available
- Consider blood cultures
- Obtain expectorated sputum culture if possible.
  - DO NOT obtain induced sputum. Endotracheal aspirate or Bronchoalveolar lavage

**IMAGING/OTHER**
- CXR or CT scan depending on clinical judgment
- Point of Care Ultrasound (POCUS)
- EKG for concern for myocardial involvement

**IMAGING**
- Chest abnormal in 60% (77% if severe)
- Chest CT abnormal in 86% (95% if severe)
- Unilateral findings on CXR or CT in 14-25% (more so if mild or early)
- Most common: Ground glass opacities, patchy consolidations >50%, peripheral distribution >50%
- Nodules, cystic changes, effusions in <10%

---

Please refer to COVID checklist in the Covid Cerner Powerplan and on Med Staff Office Website.

Consider COVID-19 in patients with any:
- Fever
- Cough
- Shortness of breath (SOB)
- High risk international or US travel/exposure

**LABS**
- CBC with diff, CMP, procalcitonin, Ferritin, CPK, CRP, LDH, ESR, D-Dimer, +/- Troponin
- Look for: leukopenia, lymphopenia and transaminitis
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**Table 1: Risk Factors For Severe COVID-19 Disease**

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Vital Signs</th>
<th>Labs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;65</td>
<td>Respiratory Rate &gt;24 breaths/min</td>
<td>Admission absolute lymphocyte count &lt;0.8</td>
</tr>
<tr>
<td>Pre-existing pulmonary disease</td>
<td>Heart rate &gt; 125 beats/min</td>
<td>CRP &gt;100</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>Sp02 &lt;90% on room air</td>
<td>LDH &gt;245</td>
</tr>
<tr>
<td>Diabetes with A1c &gt;7.6%</td>
<td></td>
<td>CRP &gt; twice upper limit of normal</td>
</tr>
<tr>
<td>History of hypertension</td>
<td></td>
<td>Elevated troponin</td>
</tr>
<tr>
<td>History of cardiovascular disease</td>
<td></td>
<td>Ferritin &gt;300 ug/L</td>
</tr>
<tr>
<td>Use of biologics</td>
<td></td>
<td>D-dimer &gt;1000 ng/ml</td>
</tr>
<tr>
<td>History of transplant or other immunosuppression</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All patients with HIV (regardless of CD4)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Adapted from Version 1 3/17/20 Massachusetts General Hospital COVID-19 Treatment Guidance

**Table 2: Suggested Treatment Algorithm Based On Clinical Severity. Refer to table 3 Medication chart.**

<table>
<thead>
<tr>
<th>Clinical Situation</th>
<th>Recommendation</th>
<th>Notes/Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>All hospitalized patients</td>
<td>Statins: continue if already prescribed. If no contraindication and for those who have a guideline indication for a statin consider starting. NSAIDS: avoid</td>
<td>Cardiovascular disease is a major risk factor for disease severity. If CPK&gt; 500 U/L, consider not starting a statin. Avoid Statins if ALT &gt;3x upper limit of normal.</td>
</tr>
<tr>
<td>Mild disease: with Sp02 &gt;90%, Upper respiratory tract infection (URTI), no risk factors</td>
<td>Supportive Care</td>
<td>See Table 1 for Risk Factors</td>
</tr>
<tr>
<td>Mild disease with Sp02 &gt;90% with risk factors for severe disease</td>
<td>Supportive care with very close monitoring. Consider hydroxychloroquine.</td>
<td></td>
</tr>
<tr>
<td>Moderate or severe disease</td>
<td>With guidance with Infectious Disease: First line: <strong>Hydroxychloroquine (Plaquenil)</strong> 400 mg BID x 1 day then 400 mg daily x 4 days + <strong>Azithromycin</strong> 500 mg daily x 5 days. In severe cases, may consider higher dose of hydroxychloroquine if available and per ID. May use chloroquine 500 mg PO BID x 7-10 days instead of hydroxychloroquine if available. Also use azithromycin.</td>
<td>Check EKG prior to initiation given risk of QT prolongation. Risk is increased in patients on other QT-prolonging agents. Keep Potassium&gt;4, Magnesium&gt;2 if concern for QT prolongation. For Hydroxychloroquine: assess for drug-drug interactions: azoles, anticoagulants, anti-epileptics. Safe in pregnancy.</td>
</tr>
</tbody>
</table>

(continued on next page)
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<table>
<thead>
<tr>
<th>Clinical Situation</th>
<th>Recommendation</th>
<th>Notes/Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>(continued from previous page) Moderate or severe disease</td>
<td>(continued from previous page) Alternative: if early in treatment course consider lopinavir/ritonavir (LPV/r or Kaletra) 400/100mg BID x 10-14 days Consider Remdesivir (RDV) through compassionate use or clinical trial if available.</td>
<td>(continued from previous page) For Protease inhibitors (Kaletra), main side effect is Gastrointestinal intolerance. Monitor liver function. Safe in pregnancy.</td>
</tr>
<tr>
<td>For certain refractory or progressively worsening patients in the ICU</td>
<td>With ID approval, interferon can be considered.</td>
<td>Can be combined with hydroxychloroquine, chloroquine, or LPV/r</td>
</tr>
<tr>
<td>For patients with evidence of cytokine release syndrome</td>
<td>With ID approval, tocilizumab can be considered</td>
<td></td>
</tr>
<tr>
<td>For patients with IgG&lt;400</td>
<td>With ID approval and for certain cases only, consider IVIG at standard dose of 1gm/kg daily x 2 doses</td>
<td>IVIG has been suggested to have anti-inflammatory or immunomodulatory effects. However, there is little rationale for this use.</td>
</tr>
<tr>
<td>For transplant patients or any other immunocompromised patients</td>
<td>Consult Infectious Disease</td>
<td></td>
</tr>
</tbody>
</table>

**OTHER MEDICATIONS**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Description</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renin angiotensin system blockers (ACE and ARBS)</td>
<td>The virus that causes COVID-19 uses the angiotensin-converting enzyme (ACE) 2 receptor to enter cells. Hypothetical harm: can increase the expression of ACE2, there is concern that these medications may facilitate viral entry into cells. Hypothetical benefit: may have protective effect against lung damage or may have paradoxical effect in terms of virus binding.</td>
<td>Currently, there is no clinical or epidemiological data to support this.</td>
</tr>
<tr>
<td>NSAIDS</td>
<td>Generally would avoid at this time with theoretical risk of worse outcome</td>
<td></td>
</tr>
<tr>
<td>Steroids</td>
<td>See next table</td>
<td></td>
</tr>
</tbody>
</table>

Adapted from Version 1 3/17/20 Massachusetts General Hospital COVID-19 Treatment Guidance
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Table 3: Experimental/Restricted Medication Chart for COVID-19 positive patients

<table>
<thead>
<tr>
<th>DRUG NAME</th>
<th>PROPOSED MECHANISM</th>
<th>BEST CANDIDATE</th>
<th>PRECAUTIONS</th>
<th>DOSING GUIDELINES</th>
<th>COST AND QUANTITY AVAILABLE (VCMC+SP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1st line therapy) HYDROXY-CHLOROQUINE (PLAQUENIL) + Azithromycin 500 mg po or IV daily x 5 days</td>
<td>Blocks viral entry into cells. Impairs viral replication. Immunomodulator.</td>
<td>Patients with moderate to severe symptoms</td>
<td>Use with caution in patients at risk for QT prolongation</td>
<td>400 mg po bid X 1 day then 200 mg po bid X 4 days + Higher doses may be recommended based on ID recommendations.</td>
<td>Cost: $ 60 on day 1 then $ 30 per day (18 tabs)</td>
</tr>
<tr>
<td>CHLOROQUINE</td>
<td>Blocks viral entry into cells. Impairs viral replication. Immunomodulator.</td>
<td>Patients with severe symptoms (1st line therapy) <strong>Use only if Hydroxychloroquine is not available</strong> (Do not give if mild symptoms)</td>
<td>Use with caution in patients at risk for QT prolongation</td>
<td><strong>Wt &gt; 50 kg:</strong> 500 mg po BID x 7-10 days <strong>Wt &lt; 50 kg:</strong> 500 mg po bid X 2 days then 500 mg po daily X 5-8 days</td>
<td>Restricted: Infectious disease approval/consult required</td>
</tr>
<tr>
<td>LOPINAVIR - RITONAVIR (KALETRA) Tablets and liquid</td>
<td>Protease inhibitor</td>
<td>Patients with severe symptoms (2nd line therapy) <strong>Alternative therapy if Hydroxychloroquine and Chloroquine are not available</strong></td>
<td>Several drug interactions. Use with caution in patients at risk for QT prolongation</td>
<td>400 mg/100 mg po bid for 10-14 days (Tablets: 200mg/50mg) (Liquid: 400mg/100mg per 5 ml)</td>
<td>Restricted: Infectious disease approval/consult required</td>
</tr>
</tbody>
</table>

Page 4  VCMC/SPH COVID-19 Clinical Working Group, Subject to Change (do not rely on print version of this document—see [http://hospitals.vchca.org/medical-staff-services](http://hospitals.vchca.org/medical-staff-services))
This algorithm is meant to provide a framework for COVID-19 treatment decision making and is subject to change as more data becomes available.

### Table 3: Experimental / Restricted Medication Chart for COVID-19 positive patients (continued)

<table>
<thead>
<tr>
<th>DRUG NAME</th>
<th>PROPOSED MECHANISM</th>
<th>BEST CANDIDATE</th>
<th>PRECAUTIONS</th>
<th>DOSING GUIDELINES</th>
<th>COST AND QUANTITY AVAILABLE (VCMC+SP)</th>
</tr>
</thead>
</table>
| DARUNAVIR (PREZISTA) + COBICISTAT (TYBOST) | Protease inhibitor  
Inhibits CYP3A resulting in increased systemic exposure of Darunavir | Patients with severe symptoms  
(2nd line therapy) | **Darunavir:** avoid if Sulfa allergy. Rash in 7% of patients  
**Cobicistat:** several drug interactions. Inhibits secretion of creatinine. | **Darunavir:** 800 mg po daily X 14 days (can be crushed)  
+  
**Cobicistat:** 150 mg po daily X 14 days (can be crushed)  
Restricted: Infectious disease approval/consult required | Cost: $ 57 per day 3/19: 360 tabs  
Cost: $ 7.5 per day 3/19: 90 tabs (backordered) |
| INTERFERON-BETA-1b (BETASERON) | Antiviral Immunomodulator | Patients with severe symptoms not responding to 1st line therapy | Precautions in patients with heart failure, hepatic disease or bone marrow suppression | 0.25 mg subcutaneously every other day for 14 days  
Restricted: Infectious disease approval/consult required | Cost: $ 570 per dose 3/19: 56 doses |
| REMDESIVIR | Blocks RNA dependent polymerase | Patients with severe symptoms  
Most likely the best therapy but available only through compassionate use or clinical trials if available | **Adverse reactions:**  
Increased liver enzymes  
Possible drug interactions | 200 mg IV on day 1  
Then 100 mg IV daily X 10 days (or until discharge)  
Restricted: Infectious disease approval/consult required | Non available at VCMC  
**Inclusion criteria:**  
Covid-19 confirmed by PCR  
Mechanical ventilation  
**Exclusion criteria:**  
Multi-organ failure  
Vasopressor requirement  
CrCl< 30ml/min or HD  
Concomitant antiviral agents  
ALT |
| TOCILIZUMAB (ACTEMRA) | IL-6 inhibitor  
Reduces IL-6 production which is a key cytokine produced in COVID-19 infections.  
No antiviral activity | Patients with severe/critical illness with rapidly worsening respiratory gas exchange and excessive inflammatory response. | **Caution if:**  
GI perforation risk  
Platelet < 100,000  
**Adverse reactions:**  
GI perforation  
Anaphylaxis  
Hepatic failure | 400 mg IV X1  
May consider an additional dose 8-12 hours later if continued clinical decompensation  
Restricted: Infectious disease approval/consult required | Cost: $ 2248 per dose 3/19: 4 vials |
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**Table 3: Experimental /Restricted Medication Chart for COVID-19 positive patients (continued)**

<table>
<thead>
<tr>
<th>DRUG NAME</th>
<th>PROPOSED MECHANISM</th>
<th>BEST CANDIDATE/ PRECAUTIONS</th>
<th>DOSING GUIDELINES</th>
</tr>
</thead>
</table>
| METHYL-PREDNISOLONE | Reduces inflammation      | **Conflicting Data:**  
|                   |                           | - **Do NOT give:**  
|                   |                           |   o Concern for increase duration of viral shedding (SARS 2004)  
|                   |                           |   o No impact on mortality (MERS, SARS)  
|                   |                           |   o WHO Recommends against.  
|                   |                           |   o Lancet article based on SARS/MERS/influenza says no  
|                   |                           | - **DO use:**  
|                   |                           |   o Wu et al 3/13/20 JAMA: yes use, 40-80 mg IV methylprednisolone daily x 3-6 days. Finally, among the patients with ARDS, of those who received methylprednisolone treatment, 23 of 50 (46.0%) patients died, while of those who did not receive methylprednisolone treatment, 21 of 34 (61.8%) died. The administration of methylprednisolone appears to have reduced the risk of death in patients with ARDS (HR, 0.38; 95% CI, 0.20-0.72; \( P = .003 \))  
|                   |                           |   o Tocilizumab trial – all used methylprednisolone  
|                   |                           | **Conclusions:**  
|                   |                           |   - Should not be used routinely.  
|                   |                           |   - If patients are going through cytokine storm (i.e. ARDS), they should get steroids.  
|                   |                           |   - If they are sick enough to get tocilizumab, they should also get steroids at above dose  

**Call Infectious Disease for approval / consult for all restricted meds**
**Emergency Department, Hospitalist and Critical Care Management**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Notes</th>
</tr>
</thead>
</table>
| **Aerosolizing procedures: avoid if possible** | • Intubation, extubation, nebulizer treatments, bronchoscopy, sputum induction (if doing for AFB; there should be no sputum induction for COVID), open suctioning of endotracheal tube, CPR  
• NOT considered high risk for aerosolization: NP/OP swab, closed suctioning from ET tube                                                                                                                                                                                                 |
| **Oxygen therapy**                  | • Oxygen up to 6 liters by nasal cannula is acceptable; higher flow has risk of aerosolization  
• Non-rebreather (NRB) may be used but higher flow rates have more chance of aerosolization (consider low flow rates ~ 6 liters per minute if possible via NRB); NRB considered a bridge to intubation |
| **High Flow Nasal Cannula (HFNC)**  | • HFNC has high potential to aerosolize, but may be considered if the following criteria are ALL met:  
  o Patient must be in a negative pressure room, and all staff entering the room must have full PPE*  
  o The patient should have a surgical mask on at all times to reduce aerosolization  
  o Flow below 30 liters (ideally 15-30 liters), for theoretical decreased risk of aerosolization  
• Should be abandoned if the patient is progressively not improving (short trials only) |
| **Adjunctive Respiratory Therapy Modalities** | • Nebulizers and Metaneb aerosolize and should be avoided in COVID suspected or confirmed infected.  
• MDIs are preferred for intubated or non-intubated patients  
• EZ Pap also likely aerosolizes, but may be considered if the following criteria are ALL met:  
  o Patient requires pulmonary toilet in order to prevent respiratory deterioration and less-invasive methods (i.e. Incentive Spirometer) have been ineffective  
  o Must be in negative pressure room if using, all staff in full PPE*  
  o Mouthpiece is used with a good seal and good understanding to minimize aerosolization  
• Patient is cooperative with all aspects of the treatment |
| **Non-invasive positive pressure ventilation (NIPPV): BiPap / CPAP** | • Generally should avoid—inevitable leak around mask ➔ aerosolization. Case-by-case with ICU consult.  
  o If using NIPPV, must use non-invasive mode on Servo-i ventilator (dedicated exhalation limb that can be filtered) and not V-60 (no exhalation limb, exhalation out the mask ➔ aerosolization)  
  o Must be in negative pressure room if using, all staff in full PPE*  
• CPAP favored over Bipap if choosing to use, less likely to aerosolize |
| **Peri-intubation**                 | • Strongly recommend intubating patients early if progressive hypoxia  
  o Variable opinion as to threshold to intubate (anywhere from 6 liters FiO2 to 75% FiO2)  
  o Silent hypoxia ➔ very high incidence of abrupt decline and need for mechanical ventilation  
  o Intubation under semi-elective conditions much preferred to emergent intubations  
• Pre-oxygenate with nasal cannula or non-rebreather (NRB): NRB lower flow rates less likely to aerosolize;  
• Avoid bagging: Option #1: Facemask to ventilator set to CPAP; Option #2 Passive bag valve mask (BVM) with viral filter, PEEP valve, O2 flow—avoid actual bagging when patient not yet intubated if possible |

*PPE: personal protective equipment; AFB: acid-fast bacilli; ET: endotracheal; NRB: non-rebreather; HFNC: high flow nasal cannula; NIPPV: non-invasive positive pressure ventilation; BiPap: bilevel positive airway pressure; CPAP: continuous positive airway pressure; FiO2: fraction of inspired oxygen; PEEP: positive end-expiratory pressure.
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### Emergency Department, Hospitalist and Critical Care Management (continued)

| Intubation | • High risk for aerosolization. Negative pressure room required if available  
|            | • Full PPE* and double-glove  
|            | • Least amount of people in room. Most experienced conductor. Least amount of attempts.  
|            | • Video laryngoscopy preferred. Disposable laryngoscope if needing direct laryngoscopy.  
|            | • Viral filter to BVM and exhalation port of ventilator  
|            | • Rapid Sequence Intubation (RSI) preferred; ensure that patient is fully paralyzed and cannot cough  
|            | • Avoid unnecessary ETT confirmatory procedures. Calculate predicted ETT depth (MDCalc) or consider standard depths (~23 inches male, ~21 inches females). Ensure black line of ETT distal to cords.  
|            | Inflate cuff, ensure viral filter on bag valve mask (BVM) before bagging/connecting to ventilator  |
| Post-Intubation Respiratory / Critical Care Management | • Before disconnecting ETT  
|            | o Sedate & paralyze patient  
|            | o Pause ventilator  
|            | o Clamp ETT (plastic clamp preferred; if metal clamp, place lots of tape around the metal that will come in contact with the tube to reduce risk tube damage)  
|            | • Closed circuit suction, Lukens trap to collect sputum for testing  
|            | • Consider waiting 45 min for CXR to allow for adequate air exchanges and reduce aerosolized particles  
|            | • Follow ARDSnet lung protective protocol (6-8 mL/kg ideal body weight for tidal volume; Plateau pressure <30 cmH2O; PaO2 >55 mmHg; SpO2 88-92%; High PEEP)  
|            | • 2 Types of ARDS have been seen:  
|            | o Typical with low compliance  
|            | o Atypical with relatively good compliance  
|            | • Consider early APRV (Airway Pressure Release Ventilation: high mean airway pressures)  
|            | Prone positioning has been shown to help if no improvement after 12-24 hr  |
| Miscellaneous Critical Care Management | • Consider placing lines after intubation to conserve PPE, reduce exposures  
|            | • Consider high incidence of myocardial suppression/shock  
|            | • Consider early discussion regarding DNR status for shock, ARDS, intubated patients  
|            | • Early Palliative Care Consult  
|            | • Code blue considerations  
|            | Consider placing ETT prior to chest compressions to avoid aerosolization  |
| Environmental | • Considered mostly droplet precautions other than high risk situations (airborne)  
|            | Surface survival times: 72 hours plastics, 48 hours steel, 24 hours cardboard, 4 hours copper  |

* Full PPE = bouffant cap, eye protection, N95 with surgical mask over it (so you can reuse the N95), gown and gloves  

**Version 1, 3/25/2020**
This algorithm is meant to provide a framework for COVID-19 treatment decision making and is subject to change as more data becomes available. Version 1, 3/25/2020

**When to consult Infectious Disease for confirmed or highly-suspected cases**

- High suspicion for COVID-19 with negative initial testing and acute respiratory failure
- Positive COVID-19 test in transplant or AIDS patients
- Positive COVID-19 test in pregnant patients
- Positive COVID-19 test and concern for secondary infections (i.e. bacterial or fungal)
- For approval / consult for restricted medications
- Anytime you have additional concerns

**References:**
Effective Treatment of Severe COVID-19 Patients with Tocilizumab, Chinese article from “Respiratory and Critical Care Medicine” 2020.
https://www.ashp.org/Pharmacy-Practice/Resource-Centers/Coronavirus
Massachusetts General Hospital COVID 19 Treatment Guidance Version 1 3/17/20
UW Medicine Interim Treatment Guidelines for SARS-CoV-2 Infection/COVID 19 Version 1.3 3/17/20
UCSF Inpatient Adult COVID 19 Interim Management Guidelines V.1 3/19/20