• This document was developed by members of the Infectious Diseases Division and pharmacy department at UPHS (in consultation with members of other divisions) to provide guidance to frontline clinicians caring for patients with COVID-19 in a non-ICU setting. It is based on a document created by Massachusetts General Hospital.
• This document provides recommendations for non-critically ill patients undergoing workup for COVID-19 or with confirmed COVID-19. It includes, but does not provide exhaustive coverage of: potential off-label and/or experimental use of medications, guidance for immunocompromised patients, suggested laboratory work up, and best practices for discharging patients. It does NOT cover recommendations for infection control, PPE, or complications of critical illness in patients with COVID-19.
• This document will be updated regularly as new data emerge. These updates will be provided on the website. As such, please do NOT download this document for clinical use at this time as this document will likely become outdated quickly.

Who Needs an ID consult?

Not all patients with COVID-19 require an infectious disease consultation.

For patients who are under investigation or who test negative, consider an ID consultation if:
  ● High suspicion of COVID-19 infection, despite negative test results

Clinical conditions that may warrant an ID consultation for patients with confirmed COVID-19 infection include:
  ● Pregnant patients
  ● Patients requiring ICU-level care or mechanical ventilation
  ● Patients with immunocompromising conditions, including but not limited to, uncontrolled HIV infection, history of solid-organ transplantation, history of bone marrow transplantation, rheumatologic disease on immuno-modulator therapy, hematologic malignancy
  ● Positive test and concern for co-infections, including viral, bacterial, or fungal
  ● Re-consultation if the patient develops ARDS, shock, or cytokine-activation syndrome

Do we need ID consultation for initiating antiviral treatment?

At present, for initiating hydroxychloroquine:
  - At HUP: ID antimicrobial approval and ID consultation are not required (New)
  - At PPMC: ID antimicrobial approval and ID consultation are not required

At present, for initiating Remdesivir:
  - For non-pregnant patients, Remdesivir is available via clinical trials only, and ID consultation is not required.
- For pregnant patients, Remdesivir may be considered for compassionate use only. ID consultation is strongly recommended.

Recommendations for all non-ICU patients with confirmed or suspected COVID-19: (Independent of decision to consult Infectious Diseases)

Table 1a: Laboratory testing suggested for patients under investigation (PUI) for COVID-19

<table>
<thead>
<tr>
<th>Obtain the following baseline labs:</th>
</tr>
</thead>
<tbody>
<tr>
<td>● SARS-CoV-2 nasopharyngeal/OP swab, with reflex to full RPP if clinically indicated (SARS-CoV2 test will run first)¹</td>
</tr>
<tr>
<td>● CBC with differential</td>
</tr>
<tr>
<td>● CMP</td>
</tr>
</tbody>
</table>

Table 1b: Laboratory testing suggested for hospitalized patients with confirmed COVID-19

<table>
<thead>
<tr>
<th>Recommended labs at baseline, to be repeated as clinically indicated²:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• CBC with differential</td>
</tr>
<tr>
<td>• CMP</td>
</tr>
<tr>
<td>• CPK (creatine kinase)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Studies at Baseline:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Baseline ECG (further Electrophysiology recommendations to follow)</td>
</tr>
<tr>
<td>• CXR (done in ED)</td>
</tr>
</tbody>
</table>

Other suggestions in caring for these patients:

- Early in hospitalization/on admission, would ensure goals of care discussions are had, including appointing POA as well as code status discussions. This should be done for all patients, but is of particular importance for those with risk factors for more severe disease and underlying comorbidities.

¹ SARS-COV Testing requires ID approval at this time. HUP: 215-614-0895  PPMC: 215-459-1406
² The clinical use of other baseline markers (D-dimer, Ferritin, LDH, CRP, ESR, among others) is not clear at this time. Recommendations for baseline labs may change with emerging data. Refer to Table 5 for further discussion of these laboratory findings.
**Suggested Therapeutics (not COVID specific)**

- Bacterial superinfection in COVID 19 patients is currently not well understood; monitor on a case by case basis.
- On admission, providers may be concerned regarding the possibility of a superimposed bacterial pneumonia - this may be based on clinical or imaging features.
  - If concerned for bacterial pneumonia and patient can produce sputum, obtain sputum culture.
  - If risk for MRSA pneumonia and you plan on empirically covering for this, you should obtain an MRSA nasal swab.
  - Based on culture results, antibiotics should be discontinued in <48 hours if there isn't evidence of a bacterial infection (this is exactly the same as management of influenza pneumonia).
- Considerations for empiric treatment for bacterial pneumonia:
  - Ceftriaxone 1 g [or cefepime if risk factors for *Pseudomonas* or multi-drug resistant organism[^4]]
  - + Doxycycline 100 twice daily for atypical coverage[^5]
  - + Vancomycin if risk factors for MRSA[^5]
- Please have a low threshold to consult ID if you are concerned about bacterial co-infection.
  - For further guidance, please refer to Pneumonia treatment guidelines and diagnostic criteria on the Antimicrobial Stewardship site: [http://www.uphs.upenn.edu/antibiotics/Community_Acquired_Pneumonia.html](http://www.uphs.upenn.edu/antibiotics/Community_Acquired_Pneumonia.html)
- For critically ill patients, consider giving empiric oseltamivir 75mg q12h while awaiting influenza and COVID testing.
- Inhaled medications should be given by metered dose inhaler rather than nebulization. Nebulization should be avoided due to risk of aerosolization of COVID 19. If nebulized medications are given, use appropriate PPE.

[^3]: Risk factors for MRSA: necrotizing pneumonia, recent viral illness, prior MRSA infection or colonization, injection drug use, End-stage renal disease

[^4]: Risk factors for *Pseudomonas* include: Structural lung disease, steroid therapy (>10 mg prednisone/day, HIV/AIDS (especially CD4<50/mL), and neutropenia (ANC<500/dL), history of multi-drug resistant organisms

[^5]: Doxycycline is now preferred over Azithromycin given anticipated shortages of Azithromycin
Clinical Trials
There are a number of clinical trials in development or enrolling inpatients with COVID-19 for treatment both at HUP and PPMC. The inclusion/exclusion criteria for the two trials that are currently enrolling are listed in Table 3. The ID clinical trials team is actively screening COVID-19 positive hospitalized patients tested in the UPHS system who are being followed by ID for enrollment in these trials. They will reach out to teams directly regarding eligibility. However, if your patient is NOT being followed by ID, they may not be on the clinical trials team’s radar. If you think a patient would qualify for a trial and you don’t need a formal ID consult, please directly reach out to the investigators below rather than paging the ID fellow.

- Kathleen Degnan at HUP: Please find contact information in UPHS phonebook (phone or email)
- Bill Short at PPMC: Please find contact information in UPHS phonebook (phone or email)

There is now a Cureatr group called “Remdesivir Clinical Trials.” If you have a patient you think may qualify for one of the Remdesivir trials, please send a message to that pool.

Please don’t alter patient treatment/testing based on the possibility of trial enrollment. If a patient is enrolled, the trial team will notify you of any necessary changes.

| Inclusion Criteria | 1. Willing and able to provide written informed consent  
|                   | 2. Aged ≥ 18 years  
|                   | 3. SARS-CoV-2 infection confirmed by PCR test ≤ 4 days before randomization  
|                   | 4. Currently hospitalized  
|                   | 5. SpO2 ≤ 94% on room air at screening  
|                   | 6. Radiographic evidence of pulmonary infiltrates |
### Inclusion Criteria

1. Willing and able to provide written informed consent
2. Aged ≥ 18 years
3. SARS-CoV-2 infection confirmed by PCR test ≤ 4 days before randomization
4. Currently hospitalized and requiring medical care for COVID-19
5. SpO₂ > 94% on room air at screening
6. Radiographic evidence of pulmonary infiltrates
7. Men and women of childbearing potential who engage in heterosexual intercourse must agree to use protocol specified method(s) of contraception

### Exclusion Criteria

1. Participation in any other clinical trial of an experimental treatment for COVID-19
2. Concurrent treatment with other agents with actual or possible direct acting antiviral activity against SARS-CoV-2 is prohibited < 24 hours prior to study drug dosing (This includes hydroxychloroquine)
3. Evidence of multiorgan failure
4. Mechanically ventilated (including V-V ECMO) for ≥ 5 days, or any duration of V-A ECMO
5. ALT or AST > 5 X ULN
6. Creatinine clearance < 50 mL/min using Cockcroft-Gault formula
7. Positive pregnancy test or breastfeeding
8. Known hypersensitivity to the study drug, the metabolites, or formulation
2. Concurrent treatment with other agents with actual or possible direct acting antiviral activity against SARS-CoV-2 is prohibited < 24 hours prior to study drug dosing. *(This includes hydroxychloroquine)*

3. Evidence of multiorgan failure

4. Requiring mechanical ventilation at time of screening

5. ALT or AST > 5 X ULN

6. Creatinine clearance < 50 mL/min using Cockcroft-Gault formula

7. Positive pregnancy test or breastfeeding

8. Known hypersensitivity to the study drug, the metabolites, or formulation

**Table 4. Special Populations**

<table>
<thead>
<tr>
<th>Solid Organ Transplant Type</th>
<th>Recommendation</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>For IgG &lt;400</td>
<td>Please consult the Transplant Infectious Diseases team if IVIg administration is being considered.</td>
<td>Major adverse event(s): VTE, infusion-related reaction</td>
</tr>
</tbody>
</table>
| For all solid organ transplant (SOT) recipients | **OUTPATIENT:** All notifications of transplant patients who are not currently inpatient (including those not seen inpatient but require follow-up) should be routed to the following email: transplantinfectiousdiseases_covid@pennmedicine.upenn.edu  
**INPATIENT:** The Transplant Infectious Diseases team should be notified of all admitted SOT recipients with confirmed COVID-19 within 24 hours of admission. | |
SOT recipients with confirmed COVID-19 and any of the following should be admitted to one of the COVID-specific services: hypoxia (SpO2 <94% on room air), radiographic evidence of pneumonia, or evidence of end-organ damage (acute kidney injury, acute liver injury, etc.).

- SOT recipients who do not meet any of the above criteria AND have a reliable follow-up plan may be discharged home.
- For any SOT recipient who is discharged home, the ED provider should send a secure message to transplantinfectiousdiseases_covid@pennmedicine.upenn.edu

<table>
<thead>
<tr>
<th>Kidney/Kidney-Pancreas</th>
<th>Asymptomatic:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>- Close monitoring</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Liver/Liver-Kidney</th>
<th>Mild-moderate disease (ie. shortness of breath/hypoxia but stable on nasal cannula):</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>- Consider Hydroxychloroquine 400mg PO q12h x 1 dose, followed by 400mg daily x 4 more days.</td>
</tr>
<tr>
<td>Heart/Heart-Liver</td>
<td>- Consider withholding cell cycle inhibitor (e.g. mycophenolate, azathioprine), if deemed appropriate by Transplant service.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Severe disease (ie. extensive PNA and/or respiratory failure requiring ICU admission):</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Consider Hydroxychloroquine (dosing as above)</td>
</tr>
<tr>
<td>- Initiate Remdesivir if enrolled in clinical trial</td>
</tr>
<tr>
<td>- Consider withholding cell cycle inhibitor (e.g. mycophenolate, azathioprine) or other modification in immunosuppression if deemed appropriate by Transplant service.</td>
</tr>
</tbody>
</table>

| Lung | - If considering pulse steroids, please consult the Transplant Infectious Diseases service. |

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Bedside respiratory care and respiratory failure management (From HUP Pulmonary/Critical Care Division Guidelines, updated 4.3.20)
- Note: There is no international, national, or local consensus on the use of High Flow Nasal Cannula (HFNC) in COVID-19 with respect to balancing clinical efficacy and healthcare worker safety. These UPHS CCC guidelines are rapidly evolving.
- Balance staff safety and standard of care for acute respiratory failure
For up to date guidance, please consult the respiratory decompensation management guidelines found at (need to be on UPHS network):

Table 5: Risk Factors for Severe COVID-19 Disease

<table>
<thead>
<tr>
<th>Epidemiological – Category 1</th>
<th>Vital Signs – Category 2</th>
<th>Labs – Category 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 65</td>
<td>Respiratory rate &gt; 24 breaths/min</td>
<td>D-dimer &gt; 1000ng/ml</td>
</tr>
<tr>
<td>Pre-existing pulmonary disease</td>
<td>Heart rate &gt;125 beats/min</td>
<td>CPK &gt; 2x upper limit of normal</td>
</tr>
<tr>
<td>Chronic Kidney disease</td>
<td>SpO2 &lt; 90% on room air</td>
<td>CRP &gt; 100</td>
</tr>
<tr>
<td>Diabetes with A1c&gt;7.6%</td>
<td></td>
<td>LDH &gt; 245 U/L</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>Admission absolute lymphocyte count &lt; 0.8</td>
</tr>
<tr>
<td>Use of biologics (presumed)</td>
<td></td>
<td>Ferritin &gt; 500 ug/L</td>
</tr>
<tr>
<td>Patients with HIV with CD4&lt;200 (presumed)</td>
<td></td>
<td>Higher SOFA Score</td>
</tr>
<tr>
<td>History of transplant of other immunosuppression (presumed)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe Obesity BMI &gt; 40</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Based on the available data from early reports out of China, a number of lab abnormalities have been identified as markers associated with development of more severe disease, including ARDS and death. In conjunction with clinical comorbidities such as underlying lung disease or diabetes, the presence of one or more of these lab abnormalities may help clinicians identify patients with poorer prognosis at an earlier stage of their infection. These lab findings, however, are non-specific and may be abnormal in patients for other reasons aside from COVID-19 infection. These tests should not be considered routine orders for all patients.

Discharge planning for COVID-19 confirmed patients

Discharge of these patients will require close coordination among clinicians, case management, infection control, and the local department of health, along with consideration of health care

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6 Only one needed to potentially denote increased risk
system capacity, laboratory testing availability, and current epidemiology. The below guidance will likely evolve as we gather more experience and data.

Discharge criteria
   ● There are no clear guidelines on when it is safe to discharge a patient with COVID-19.
   ● Patients may be considered for discharge when they are:
      ○ hemodynamically stable
      ○ fever is improving (do not need to be afebrile)\(^7\)
      ○ other symptoms are improving
      ○ oxygen requirement is declining or resolved
      ○ they have capacity to perform basic ADLs, or ambulate in room, or are at baseline functional status
   ● Communication with expert consultants may be indicated to determine if a high-risk patient (e.g. immunosuppressed, transplant, HIV+, pregnant patient) requires specific post-discharge care

Options for Home Monitoring after discharge from hospital:

Currently, “default” option for **ALL** patients with COVID-19 being discharged home from the hospital who do not qualify for the more intensive homecare options below (NOTE: not yet available at LGH):
   ● Penn Medicine On Demand through **COVID Watch** Program:
      ○ Program that texts patients twice daily to “Is breathing better, worse, or the same?”-if patient selects worse to this and follow up question→ triggers RN call with escalation pathway to MD
      ○ Patients can contact system 24 hours a day via text
      ○ To enroll upon discharge: Click “More-->Rarely used” in left hand EPIC menu--> click “Way to health” button: Enroll. Choose Watch program. The provider must enter a working patient phone number. Enrolls patients upon discharge, but patients will receive text within 30 seconds of enrollment. Enrollment lasts for 14 days, but can be extended for an additional 7 days. This program is now live.
      ○ For more information: [https://covidwatch.waytohealth.org/](https://covidwatch.waytohealth.org/)
      ○ More detailed instructions will be available from floor case manager and on website

For patients with more significant home care needs (see criteria below):
   ● Penn Medicine at Home: this is more intensive home nursing care, either via telehealth visits with monitoring of vitals or in person visit (with appropriate PPE):
      ○ Skilled nursing needs (chest tube, wound care.)

\(^7\) Median duration of fever was 12 days in Zhou Lancet doi: 10.1016/50140-6736(20)30566-4
○ Need for close monitoring of pulse oximetry and other vital signs due to underlying illnesses (lung disease, heart failure, etc.)
○ Have been started on home oxygen for COVID-19.
○ Contact floor case manager to provide referral and ensure eligibility
● Penn Medicine Hospice Care
  ○ For patients with poor prognosis who have opted for comfort care in their homes
  ○ Contact floor case manager to provide referral and ensure eligibility

Discharge checklist

Discharge location

- Inquire about residence, preferably with private room, ability to adhere to home isolation instructions, and risk of transmission to persons with immunocompromising conditions in the home
- Verify and document contact number for patient and primary support person. Ensure active phone service, voicemail functioning, and language preference correctly documented
- Verify ability to manage ADL/iADLs with adequate support at home
- Confirm patient has resources/social support to receive 1-2 weeks of food and other necessary supplies while undergoing quarantine
- Perform DME needs assessment and consider sponsorship of DME from hospital if items unable to be delivered to home or obtained by social support person
- Patients returning to congregate settings after discharge (e.g. skilled nursing facility, hemodialysis center) require additional considerations. Infection control experts should provide guidance on lab testing requirements and symptom management that is necessary for patients to return to these locations
- Patients who are homeless or have unstable housing will require close coordination with the department of public health to identify an alternate living situation and may require mobilization of local resources

Discharge medications & supplies

- Provide at least a 14-day supply of medications to cover duration of home isolation, or confirm 14 day supply at home
- Provision of hydroxychloroquine, if initiated while inpatient, will be determined by supply in outpatient pharmacy and assessment of underlying cardiac risk (including baseline QTC, as likely unable to monitor daily in outpatient setting). This should be decided on a case by case basis by primary team.
- Provide a surgical mask as available to infected patients who are being home where there are other family members

Transportation

- Verify the patient has a ride by private vehicle. If not available, engage floor case manager to arrange transportation (infected person should wear a mask in vehicle)
Discharge instructions

- Provide return precautions for evaluation of concerning symptoms after discharge, such as fever and/or worsened respiratory symptoms. Enroll patients in either COVID Watch, or if appropriate, Penn Medicine at Home.
- Provide patient with home isolation instructions
  - Instructions for the patient can be found at the pdf below. If repeat testing to confirm clearance of the virus is not being performed, the patient must remain in home isolation until afebrile for at least 72 hours without antipyretics AND improvement of symptoms AND at least 7 days from onset of symptoms. [https://www.cdc.gov/coronavirus/2019-ncov/downloads/sick-with-2019-nCoV-factsheet.pdf](https://www.cdc.gov/coronavirus/2019-ncov/downloads/sick-with-2019-nCoV-factsheet.pdf)

List of Abbreviations Used:

HFNC - High flow nasal cannula
NPPV - Non-invasive positive pressure ventilation
NRB - Non-rebreather Mask
PEFR - Peak Expiratory Flow Rate
PUI - person under investigation
SOT - solid organ transplant