COVID 19 ID Clinical Guidelines for Non-ICU Patients
Last Revised: 7.4.20

• 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 documents created by Massachusetts General Hospital and University of Washington.
• 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 As such, please do NOT download this document for clinical use at this time as this document will likely become outdated quickly.**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 (no longer recommended outside of clinical trials):

- At HUP: ID antimicrobial approval and ID consultation are not required
- At PPMC: ID antimicrobial approval and ID consultation are not required

At present, for initiating Remdesivir:

- For pregnant patients, Remdesivir may be considered for compassionate use only. ID consultation is strongly recommended.

- For patients not involved in clinical trials, emergency use of Remdesivir is available on a limited, case by case basis (added 5.19.20)

Day and Time	HUP Procedure	PPMC Procedure
Weekdays 8a-5p	Contact the antibiotic stewardship team through the ILÚM app or web-based software and request remdesivir similar to other restricted antibiotics (for instructions on use of ILÚM go to the following link: http://www.uphs.upenn.edu/antibiotics/antibiotic_approval/index.html). Initial triage for remdesivir allocation will be performed by the antibiotic stewardship team. If patients are able to receive an allocation of remdesivir, the antibiotic stewardship team will contact the treating team and trigger an official infectious diseases consultation as a condition to receive EUA remdesivir.	
Weekends and Holidays 8a-5p	Contact the antibiotic stewardship team through ILÚM as above, and the process will work as described on weekdays.	Contact the antibiotic stewardship team through ILÚM **AND** request an official infectious diseases consultation. These groups will discuss and determine the potential allocation of remdesivir.
Sunday 5p-8a Monday 5p-8a Tuesday 5p-8a Wednesday 5p-8a Thursday 5p-8a	Contact the antibiotic stewardship team through ILÚM as above. The request will be in the queue for review when the antibiotic stewardship is available at 8a the following morning. Receipt of remdesivir is **not an emergency** so it will not be administered as a stat dose overnight. Initial triage for remdesivir allocation will be performed by the antibiotic stewardship team. If patients are able to receive an allocation of remdesivir, the antibiotic stewardship team will contact the treating team and trigger an official infectious diseases consultation as a condition to receive EUA remdesivir.	
Friday 5p-8a Saturday 5p-8a Night before holiday 5p-8a	Contact the antibiotic stewardship team through ILÚM as per weekday and non-holiday evenings as above, and the process will work as described on these days.	Contact the antibiotic stewardship team through ILÚM at any time **AND** request an official infectious diseases consultation after 8a the following morning, and the process will work as described on weekend and holiday days.

*** A request for remdesivir submitted through these channels at HUP and PPMC does not constitute approval for remdesivir so should not be framed to patients as such. Allocation depends on supply and patient eligibility as determined by infectious diseases consultation.** For any questions or concerns, contact Keith Hamilton (HUP) or Naasha Talati (PPMC).

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
Obtain the following baseline labs: ● SARS-CoV-2 nasopharyngeal/OP swab, with reflex to full RPP if clinically indicated

(SARS-CoV2 test will run first)[1]
- CBC with differential
- CMP

Table 1b: Laboratory testing suggested for hospitalized patients with <u>confirmed</u> COVID-19

<u>Recommended labs at baseline, to be repeated as clinically indicated[2]:</u>
- CBC with differential
- CMP
- CPK (creatine kinase)
- Pregnancy Test (for women of childbearing age)

<u>Studies at Baseline:</u>
- Baseline ECG (further Electrophysiology recommendations to follow)
- CXR (done in ED)

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.

<u>Suggested Therapeutics (not COVID specific)</u>

- 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

[1] SARS-COV Testing of symptomatic patients 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.

    - If risk for MRSA pneumonia[3] 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

- 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.

Table 2. Suggested COVID-19 Specific Treatments based on Clinical Situation

Link to UPHS Treatment Guidelines: https://pennmedaccess.uphs.upenn.edu/f5-w-687474703a2f2f7777772e757068732e7570656e6e2e656475$$/antibiotics/COVID19.html

Table 3. 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 below. 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*

[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

don't need a formal ID consult, please directly reach out to the investigators below rather than paging the ID fellow.

- Various Contact People at HUP (please see below for specific trials): Please find contact information in UPHS phonebook (phone or email)
- Bill Short at PPMC: Please find contact information in UPHS phonebook (phone or email)

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. An updated list of ongoing clinical trials is found here (scroll until you see the colorful boxes):

https://pennmedaccess.uphs.upenn.edu/f5-w-687474703a2f2f7777772e757068732e7570656e6e2e656475$$/antibiotics/COVID19.html

Table 4. Special Populations		
Solid Organ Transplant Type	**Recommendation**	**Notes**
For IgG <400	Please consult the Transplant Infectious Diseases team if IVIG administration is being considered.	Major adverse event(s): VTE, infusion-related reaction, acute kidney injury
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	
Kidney/Kidney-Pancreas **Liver/Liver-Kidney** **Heart/Heart-Liver**	Asymptomatic: - Close monitoring Mild-moderate disease (ie. shortness of breath/hypoxia but SpO2 >90% on nasal cannula): - Consider reducing or withholding cell cycle inhibitor (e.g. mycophenolate, azathioprine), if deemed appropriate by Transplant service. Severe disease (ie. extensive PNA and/or respiratory failure requiring ICU admission): - Consider withholding cell cycle inhibitor (e.g. mycophenolate, azathioprine) or other modification in immunosuppression if deemed appropriate by Transplant service.	Consider referring for clinical trial or expanded access with convalescent plasma or clinical trial with hydroxychloroquine or remdesivir-containing regimen if patient qualifies (see footnotes in table above)
Lung	- If considering pulse steroids, please consult the Transplant Infectious Diseases service.	Consider referring for clinical trial or expanded access with convalescent plasma or clinical trial with hydroxychloroquine or remdesivir-containing regimen if patient qualifies (see footnotes in table above)

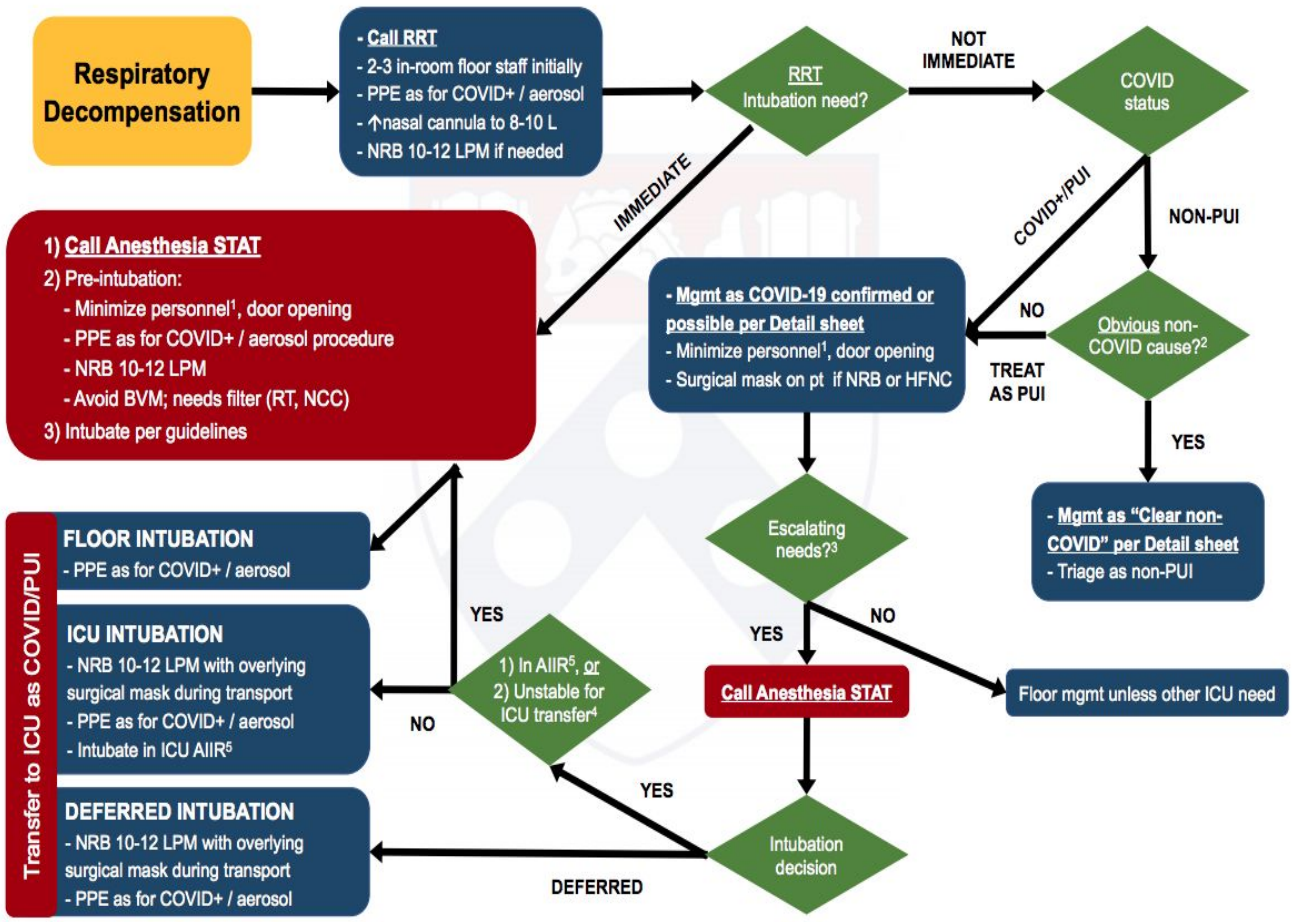
Click on the following hyperlink for: Details on drug interactions with immunosuppressants and experimental COVID-19 therapies *(University of Liverpool)* (pg 26 of 29)

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
- Many respiratory interventions may cause aerosolization and pose a risk to healthcare workers and bystanders. Aerosol generating procedures are currently thought to include: 1. Intubation 2. NPPV 3. Nebulizer therapies 4. Extubation 5. HFNC 6. Masks – Venturi, NRB, BMV 7. Bronchoscopy 8. Sputum induction 9. Open suctioning 10. Trach collar 11. Tracheostomy/trach change 12. NGT placement 13. Cough assist/Chest PT 14. PEFR, FVC/Spirometry

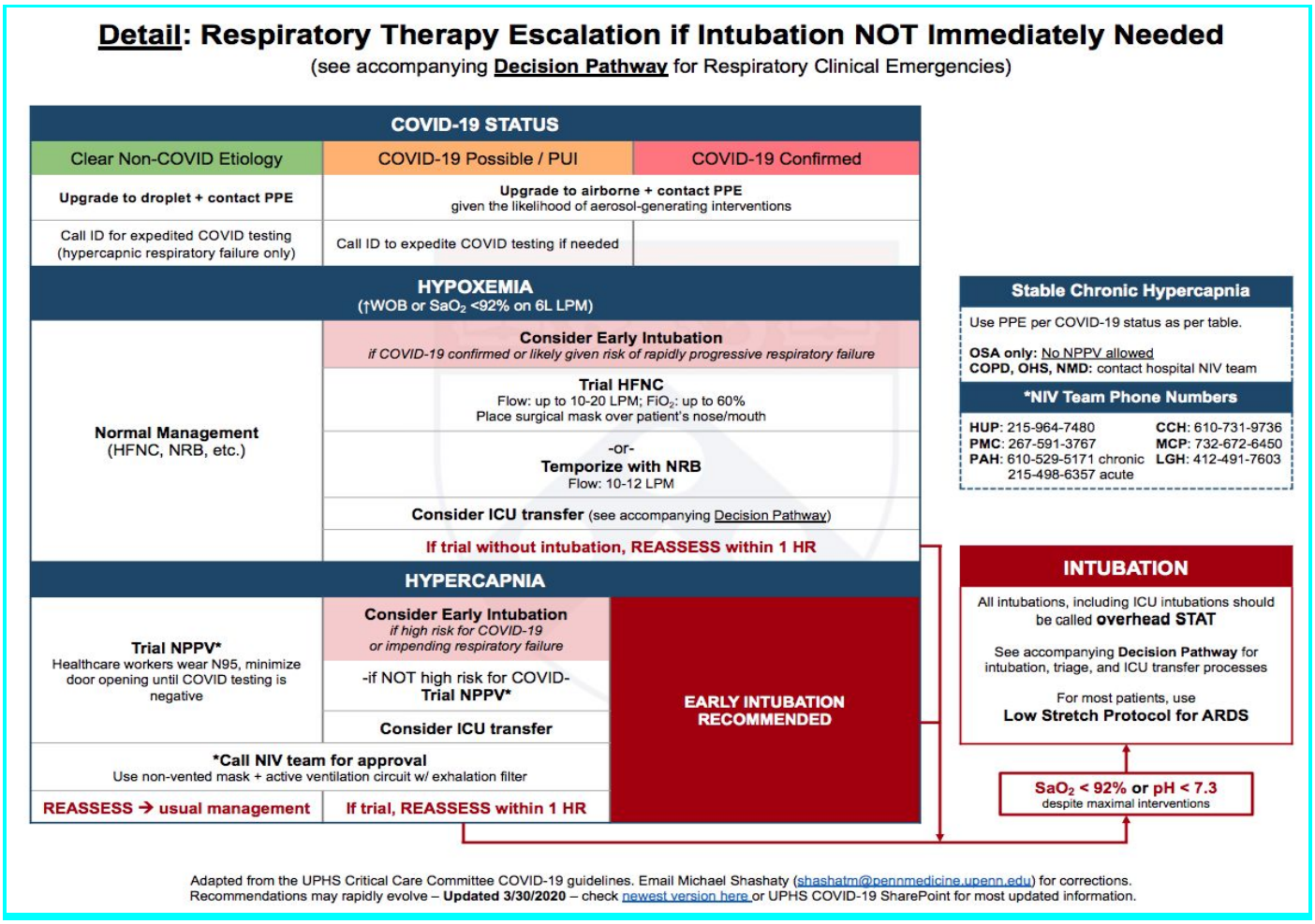
Decision Pathway: Respiratory Clinical Emergencies

(see accompanying **Detail** sheet)



[1]Anesthesia (1-2); Nurse (1); RT (1); RRT provider (1) [2]E.g. witnessed aspiration [3]Persistent higher O_2 needs, ↑work of breathing [4]Plan for ↑ transport time for PUIs
[5]PAirborne Infection Isolation Room, i.e. negative pressure room

Pathway adapted from the UPHS Critical Care Committee COVID-19 guidelines. Email Michael Shashaty (shashatm@pennmedicine.upenn.edu) for corrections.
Recommendations may rapidly evolve – **Updated 3/30/2020** – check newest version here or UPHS COVID-19 SharePoint for most updated information.



For up to date guidance, please consult the respiratory decompensation management guidelines found at (need to be on UPHS network):

https://pennmedaccess.uphs.upenn.edu/f5-w-687474703a2f2f6163636573737370f696e742e757068732e7570656e6e2e656475$$/sites/preparedness/coronavirus/_layouts/15/WopiFrame.aspx?sourcedoc=/sites/preparedness/coronavirus/Critical%20Care/Updated%203-27-20%20Overall%20ICU%20Management%20and%20Resp%20Care%20with%20COVID%2019.%20pdf.pdf&action=default

Table 5: Risk Factors for Severe COVID-19 Disease [6]		
Epidemiological – Category 1	*Vital Signs – Category 2*	*Labs – Category 3*
Age > 65	Respiratory rate > 24 breaths/min	D-dimer > 1000ng/ml
Pre-existing pulmonary disease	Heart rate >125 beats/min	CPK > 2x upper limit of normal
Chronic Kidney disease	SpO2 < 90% on room air	CRP > 100
Diabetes with A1c>7.6%		LDH > 245 U/L
History of hypertension		Elevated troponin
History of cardiovascular disease		Admission absolute lymphocyte count < 0.8
Use of biologics (presumed)		Ferritin > 500 ug/L
Patients with HIV with CD4<200 (presumed)		Higher SOFA Score
History of transplant of other immunosuppression (presumed)		
Severe Obesity BMI > 40		

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

[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/
    - 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-fact-sheet.pdf
    - ❏ Instructions for household members can be found here: https://www.cdc.gov/coronavirus/2019-ncov/hcp/guidance-prevent-spread.html

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