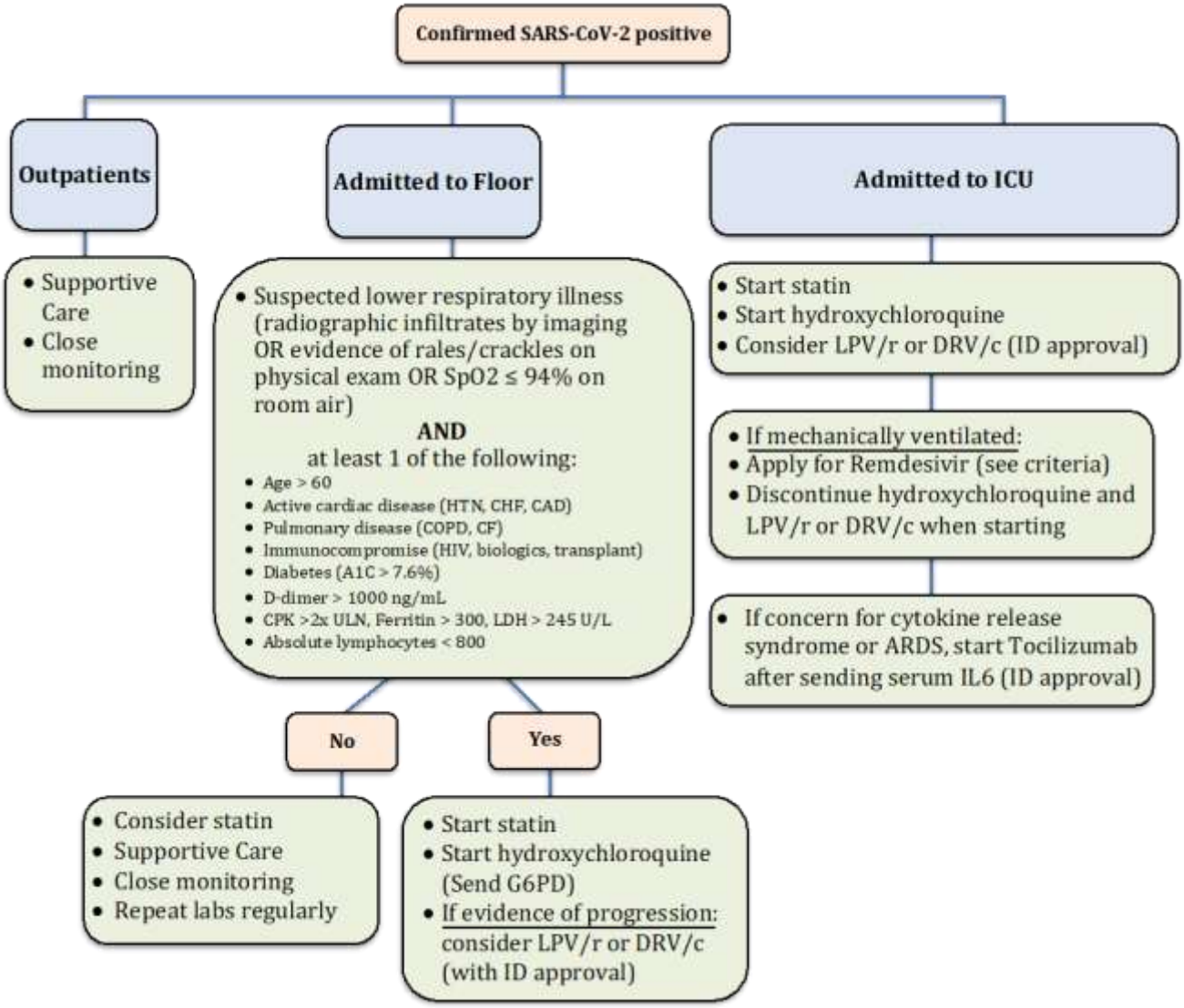
- This document is designed to assist clinicians in the treatment of confirmed COVID-19 infection in hospitalized patients.
- **No standard treatment has been proven or endorsed currently by the CDC or WHO.[1]**
- All therapies are deemed experimental at this time based on published cases and early trial results from outside the US. [2-9]
- Supportive care remains the cornerstone of therapy.
- An Infectious Diseases consult is strongly recommended for confirmed COVID-19 cases as many therapies require compassionate use sign off or trial enrollment.
- This document does NOT cover recommendations for management of hypoxemia, fluid resuscitation or other complications in patients with COVID-19.
- Please note when this document was last updated. Updates will occur in real time as data emerge.

Figure 1: Summary Flow Chart of Treatment



Laboratory Testing and Radiology

*Note: Given limited drug supplies, specific guidance in this document is intended only for **COVID-19 confirmed patients**. If the patient has not yet been tested for SARS-CoV-2*, approval for testing may be obtained through the BIDMC HID Pager (33860)

Table 1: Tests for Hospitalized Patients with Confirmed COVID-19

Daily Laboratory Testing • CBC with diff (trend total lymphocyte count) • Complete metabolic panel • Liver function tests (ALT/AST/tbili) For risk stratification (may be repeated if abnormal or with clinical deterioration): • CPK (creatine kinase) • D-dimer • Ferritin • LDH • Troponin[2] • IL-6 for ICU patients Viral serologies:[1] • HBV serologies (sAb, cAb, and sAg) • HCV antibody, unless positive in past • HIV 1/2 Ab/Ag G6PD testing (in case hydroxychloroquine is required) Immunocompromised patients: If clinically indicated, consider serum beta-d-glucan to evaluate for *Pneumocystis.* (Do not routinely induce sputum given risk of aerosolization; yield from non-induced sputum is low).	Radiology: • Portable CXR at admission • High threshold for PA/lateral in ambulatory patients, consider only if low suspicion for COVID-19 and result would change management or affect PUI status. Baseline ECG[3] • If starting QTc prolonging drug, can repeat ECG in 24-48 hours to monitor QTc. If baseline QTc > 500, repeat within 24 hours and consider stopping QTc prolonging drugs. If clinically indicated: • Routine blood cultures (2 sets) • For acute kidney injury (i.e. serum creatinine >0.3 above baseline), send urinalysis and spot urine protein:creatinine

[1]Viral serologies assist for interpretation of ALT elevations, present in ~25% of presentations.
[2]Elevated troponin (> 2 times upper limit of normal) without hemodynamic compromise, can repeat troponin in 24 hours and echocardiogram not necessary. Uptrending troponin with hemodynamic compromise or other concerning cardiovascular symptoms /signs should prompt consideration of obtaining an echocardiogram.

Non-COVID-19 Therapeutics:

- Symptomatic care:
  - Antitussive agents
  - Expectorants
  - Acetaminophen (avoid NSAID's if possible)
- Inhaled bronchodilators should be given by metered dose inhaler rather than nebulization
  - Nebulization risks aerosolization of SARS-CoV-2
  - If out of inhalers, use appropriate PPE for nebulizers
- Empiric treatment if concern (radiographic) for bacterial pneumonia:
  - Ceftriaxone 1 g [or antipseudomonal beta lactam if ICU or MDR risk factors] + Azithromycin 500 mg x1, then 250 mg daily x 4 days + Vancomycin if risk factors for MRSA
  - Duration guided by microbiology and MRSA screen

Not recommended

- **Systemic steroids** should in general be avoided given potential harm. Steroids may be considered if indicated for another reason. A randomized controlled trial is testing the safety/efficacy of steroids for COVID-19 (NCT04273321). Until results are available, broad use of steroids, especially in milder forms of the disease, is discouraged.
- **Ribavirin** is not recommended at this time.
- **NSAID** use has been reported preceding clinical deterioration in some patients with severe COVID-19 disease. Providers should assess recent NSAID use and avoid prescribing NSAIDs while patients are admitted.

Unknown or Neutral

- **ACE-Inhibitors (ACEi) / Angiotensin Receptor Blockers (ARBs):**
  - SARS-CoV-2 virus binds to the ACE2 receptor for cellular entry. It is unknown if these agents either help or worsen COVID-19 disease.
  - Currently there are no data to support either starting or stopping ACEi/ARBs on any patients with COVID-19. However, if acute kidney injury, hypotension or other contraindication develops, we recommend stopping them at that time.
- **Inhaled steroids:** These agents may reduce local immunity and promote viral replication, but this consideration must be balanced by potential benefits for management of reactive airways.

Recommended

Step 1: Identify Risk Factors

Table 2: Risk Factors for Severe COVID-19 Disease

Demographic	*Labs*
-Age > 60 -Pre-existing pulmonary disease -Chronic kidney disease -Diabetes with A1c > 7.6% -History of hypertension -History of cardiovascular disease -Use of biologics -History of transplant or other immunosuppression -All patients with HIV (regardless of CD4 count)	-D-dimer > 1000 ng/mL -CPK > twice upper limit of normal -CRP > 100 -LDH > 245 U/L -Elevated troponin -Admission lymphocyte count < 800 -Ferritin > 300 ug/L

Step 2: Treat Based on Severity

Table 3: Suggested Treatment Algorithm Based on Clinical Severity

Clinical Situation	*Recommendation*	*Notes / Considerations*
All hospitalized patients (regardless of severity)	May consider use of a statin (see below)	Close monitoring for progression
Patients requiring floor admission with suspected lower respiratory disease (radiographic infiltrates by imaging OR evidence of rales/crackles on physical exam OR SpO2 ≤ 94% on room air) AND at least one additional risk factor (see Table 2)	Start statin atorvastatin 40 mg daily Start hydroxychloroquine (400 mg BID x2 followed by 400 mg daily while hospitalized for up to 5-10 days). Note chloroquine has activity but limited supply so hydroxychloroquine preferred If evidence for progression: With ID approval, consider: lopinavir/ritonavir (LPV/r or Kaletra) 400/100 mg BID for 10 days If LPV/r not available, consider using darunavir/cobicistat (DRV/c) 800/150 mg daily	Avoid if elevated CPK (>/= 2x ULN) or ALT > 3x upper limit of normal Check ECG prior to HCQ initiation given risk of QT prolongation. Risk is increased in patients on other QT-prolonging agents. Do not use if QT > 500 msec. Avoid in myasthenia gravis, porphyria, retinal pathology, epilepsy. Pregnancy is not a contra-indication. Assess for drug-drug interactions before starting. Main HCQ side effect is gastrointestinal intolerance. Monitor liver function tests while on therapy.
Patients requiring ICU admission	Manage as above. If mechanically ventilated: obtain Remdesivir (RDV) through compassionate use Current dosing of RDV is 200 mg IV loading dose following by 100 mg IV daily for up to 10 days. Discontinue hydroxychloroquine and any other other antiviral agent when starting Remdesivir	For compassionate use, apply through portal here: https://rdvcu.gilead.com Exclusion criteria: Evidence of multiorgan failure, on pressors, creatinine clearance < 30, transaminases > 5X ULN, concomitant use of other antivirals
Patients with suspected cytokine release syndrome (elevated IL-6 >40 pg/mL), and/or concern for developing or existing ARDS; supported by D-dimer > 1000 ng/mL, CRP > 100.	With ID approval, consider Tocilizumab (Actemra) 400 mg IV once OR 8 mg/kg intravenously (maximum 800 mg/dose) infused over an hour	Need to send serum IL6 level (senout to Mayo clinic) prior to giving first dose of tocilizumab Avoid if transaminases >5x ULN, ANC < 500, Plts < 50 See also: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30628-0/fulltext?rss=yes

Table 4: Special Populations		
	Recommendation	**Notes**
Solid organ and BMT recipients	Guided by transplant and transplant ID teams – please call/consult Request bronchoscopy only if significant decompensation, versus lung biopsy as may be lower risk for aerosolization and exposure to staff Reduction of immunosuppressants need to be considered with guidance by transplant and transplant ID teams.	Screen for drug-drug interactions with anti-viral agents, if they are being used
If IgG <400	Consider IVIG at standard dose of 1 gm/kg daily x 2 doses	

Agent/dosing	**Target / Mechanism**	**Dosing**	**Monitoring**
Atorvastatin (Lipitor)	Cardioprotection; immunomodulatory. May help promote antiviral innate immune response	20-40 mg PO daily	CPK for potential elevation, myalgia, weakness
Hydroxychloroquine (Plaquenil)	Multiple actions; prevents binding to ACE2, presents transport in endosome, and possibly others	400 mg PO BID x 2 doses, then 400 mg PO daily for 5- 10 days	EKG baseline: QTc prolongation: Switch to PI based therapy or avoid if QT>500 msec Use caution in acute or chronic kidney disease
Lopinavir/ritonavir (LPV/r or Kaletra)	3CLpro (viral protease) inhibitor	400/100 mg PO BID x 10days (liquid permitted if intubated ONLY)	LFT's, drug-drug interactions (LPV/r) potent cytochrome P450 enzyme inhibitor
Darunavir/cobicistat (DRV/c)	3CLpro (viral protease) inhibitor	800mg/150mg po daily x 10 days	LFT's, drug-drug interactions (LPV/r) potent cytochrome P450 enzyme inhibitor
Remdesivir	RNA-dependent RNA polymerase inhibitor	200 mg IV x1, then 100 mg IV daily, up to 10 days	ALT elevations, hypersensitivity
Tocilizumab (Actemra)[1]	Monoclonal antibody to IL6 receptor / treats cytokine release syndrome	400 mg IV once[9] OR 8 mg/kg IV (max 800 mg)	AST/ALT elevations, infectious complications (TB/Hepatitis), hypersensitivity

[1] Use caution in patients with IBD for perforation risk.

Liverpool COVID-19 Drug Interactions

UCSF Protease inhibitor drug interactions:

Post-exposure Prophylaxis for Healthcare Workers

- There is currently no data for post-exposure prophylaxis for people with a known COVID-19 exposure. Exposed persons should follow self-quarantine for 14-days and monitor for symptoms. Healthcare workers should follow instructions from Occupational Health.
- As of 3/18/20, healthcare workers and close household contacts may be eligible to enroll in a clinical trial for post-exposure prophylaxis if within 3 days of exposure; inquiries should be sent to: covid19@umn.edu

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