1.1 Clinical Spectrum

Covid-19 infection: Individuals who test positive for SARS-CoV-2 using a virological test (i.e., a nucleic acid amplification test [NAAT] e.g., RT-PCR or an antigen test)

Severity indicators

Asymptomatic	No symptoms
Mild disease	Fever, cough (usually dry), sore throat, malaise, headache, myalgia, diarrhea, vomiting, loss of taste or smell, anorexia, but no dyspnea; normal O2 saturation and normal chest X-ray
Moderate disease	Evidence of lower respiratory tract infection (exam and/or imaging), O2 saturation ≥94% on room air
Severe disease	Symptoms of moderate disease but O2 saturation <94%, PaO2/FiO2 <300 mmHg, respiratory frequency >30 breaths per minute, or lung infiltrates >50%
Critical disease	Symptoms of severe disease but intubated with respiratory failure, septic shock, and/or multiorgan dysfunction

Stratification of Risk Factors and predictors of severe disease[1,2]

Patients with higher risk of progression to severe COVID-19, should be monitored closely until clinical recovery is achieved

Epidemiological Category	Vital Signs	Labs & image
Age ≥ 60 years	Respiratory rate > 30 breaths/min	D-dimer > 1000 ng/ml
Pre-existing pulmonary disease	Heart rate > 125 beats/min	CPK > twice upper limit of normal
Chronic Kidney or Liver disease	SpO2 <94% on room air	CRP ≥ 75 mg/L
Obesity (BMI ≥ 30)		Elevated troponin
Tobacco use disorder		LDH > 245 U/L
Diabetes		Lymphocytopenia and leukopenia (Ratio of absolute neutrophil count to absolute lymphocyte count > 3.5)

Epidemiological Category	Vital Signs	Labs & image
Pregnancy		Ferritin > 500 ug/L
History of Cardiovascular Disease (including Hypertension)		High serum IL-6 level
History of cerebrovascular disease		Acute Kidney Injury (increase Cr)
Solid organ or stem cell transplant		Thrombocytopenia
Immunocompromised state: acquired or congenital		LFT > 5 times upper normal limit
HIV infection		SOFA > 5
Neurological diseases		Infiltrate on CXR > 50%
Cancer		
Tuberculosis		
Substance use disorder		
Sickle cell disease and thalassemia		
Down's syndrome		

1.2 Initial investigations

1.2.1 Non-hospitalized patients

- **Asymptomatic/mildly symptomatic low-risk patients**: perform investigations if indicated
- **Asymptomatic/mildly symptomatic high-risk patients** will only need CBC, Metabolic panel, CRP, Baseline CXR, and baseline ECG

1.2.2 Hospitalized patients[3,4] (table 1)

Table 1 Investigations for COVID-19 confirmed patients

CBC with differential	Ferritin	ECG
Comprehensive metabolic panel	CK	Inflammatory markers (e.g., CRP)
Troponin*	Coagulation screen + D-Dimer	LDH
CXR		
When indicated		
ABG	Pneumonia PCR panel	Blood and Sputum Culture
Respiratory viral panel	MRSA nasal screening	MDRO screening
Procalcitonin	IL-6	B-HCG for women in childbearing age
Triglycerides		

*Elevated troponin (> 2 times upper limit of normal) without hemodynamic compromise, can repeat troponin in 8-12 hours. Up-trending troponin with hemodynamic compromise or other concerning cardiovascular symptoms signs should prompt consideration of obtaining an urgent cardiology consultation

1.3 Management [5-7,10]

Important note: date of symptoms onset should drive treatment decision making (not the date of first positive test)

Table 2 Management guidance for confirmed SARS-CoV-2 infection

Non-hospitalized asymptomatic, or mild-moderate disease **Not at high risk of disease progression**	• Isolation • Supportive Care: Treat symptoms (eg, antipyretics for fever/pain, adequate nutrition, appropriate rehydration, sleeping meds (e.g., melatonin) as needed • Do not initiate anticoagulants or antiplatelet prophylaxis therapy unless other indications exist

Non-hospitalized, mild-to-moderate disease **High risk of disease progression**	• Monoclonal antibodies: Sotrovimab[8,19,20] 500 mg single I.V infusion within 5-10 days of symptoms onset. It retains activity against wild-type and all tested variants of concern including Omicron. • Oral antivirals (Molnupiravir or Paxlovid) once approved and authorized • Do not initiate anticoagulants or antiplatelet prophylaxis therapy unless other indications exist
Hospitalized for non-COVID-19 related condition: **asymptomatic COVID-19 or mild symptoms**	• Similar management to non-hospitalized COVID-19 cases • + Prophylactic anticoagulant
Hospitalized, moderate disease (Evidence of lower respiratory tract disease) with no supplemental O2 requirement. Patient at high risk of disease progression	• Remdesivir [9] • Prophylactic anticoagulation • Dexamethasone NOT recommended
Hospitalized, severe disease, requires supplemental O2	• Remdesivir [9] • Dexamethasone • Prophylactic anticoagulation • Tocilizumab if CRP ≥ 75 with progressive disease. *Baricitinib: May be used in combination with Remdesivir where a corticosteroid cannot be used. May also be used in place of Tocilizumab in combination with a corticosteroid; should not be used in combination with Tocilizumab
Hospitalized, critical disease-requires mechanical ventilation or ECMO	• Dexamethasone • Tocilizumab if CRP ≥ 75 with progressive disease • Prophylactic anticoagulation • +/- Remdesivir (benefit unproven) *Baricitinib: May be used in combination with Remdesivir where a corticosteroid cannot be used. May also be used in place of Tocilizumab in combination with a corticosteroid; should not be used in combination with Tocilizumab

1.3.1 The committee recommend against treatment of COVID-19 cases-outside clinical trials-with

- (Hydroxy)chloroquine
- (Hydroxy)chloroquine + azithromycin
- Lopinavir/ritonavir (Kaletra)
- Famotidine
- Ivermectin

1.3.2 Insufficient data to recommend for or against

- Anakinra
- Colchicine
- IFN-β
- Favipiravir
- Inhaled Budesonide
- Tofacitinib
- Convalescent Plasma

1.3.3 Management principles of all COVID-19 patients [5-7,10]

- Adhere to infection prevention measures
- The main standard treatment for SAR-CoV-2 remains supportive care
- Airborne precaution is required for all patients undergoing aerosol generating medical procedures, including nebulizer treatment
- If inhaler medications are needed, use MDI and spacer device
- In hypoxic patients, we strongly recommend the use of rotating or proning as a valuable tool in improving oxygenation and decreasing respiratory effort in many patients with moderate or severe COVID-19. Care must be taken to not disrupt the flow of oxygen during patient rotation, but we recommend proning regardless of oxygenation modality. Typical protocols include 30-120 minutes in prone position, followed by 30-120 minutes in left lateral decubitus, right lateral decubitus, and upright sitting position. Positioning is guided by patient comfort and are is generally evaluated within 5-10 minutes in a new position; do not maintain a position that does not improve the patient's breathing and comfort

1.3.4 Anticoagulation

- All hospitalized adults with COVID-19 who are not critically ill (non-ICU patients) should receive **prophylactic** dose anticoagulation with LMWH **regardless** of COVID-19 disease severity, if not contraindicated [22]. (For dosing see table 3).
  Contraindications include active bleeding or platelet count less than 25,000; monitoring advised in severe renal impairment; abnormal PT or APTT is not a contraindication. If LMWH is contraindicated due to renal failure (Cr Clearance < 30mL/min), Unfractionated Heparin 5000

units SC q12 can be used as an alternative. Fondaparinux is preferred in those with heparin-induced thrombocytopenia. For patients with high risk of severe illness as defined by D-dimer > 4 folds of the upper limits of normal we strongly suggest using therapeutic dose of anticoagulation (UFH or LMWH) according to most recent randomized control trials [23-25]. When feasible and safe, we strongly support use of CTA to rule out pulmonary embolism given high propensity of thromboembolic disease in COVID-19 patients.

- Patients with mild COVID-19 disease in the ER should not have coagulation markers routinely measured as they will not receive any form of antithrombotic regardless of D-Dimer levels.
- All hospitalized critically ill (ICU) patient should receive prophylactic dose of anticoagulation with LMWH or unfractionated heparin in case of severe renal impairment or fondaparinux in case of HITT
- **Full (therapeutic) dose anticoagulation** in critically ill (ICU patient) is indicated in the following scenarios:

    - Documented VTE (PE, or DVT, Echo findings of clot in transit, or vascular access device thrombosis)
    - Suspected VTE in which confirmatory testing is not possible such as:

        1. Sudden deterioration in respiratory status when chest radiography and/or inflammatory markers are stable or improving and the change cannot be attributed to a cardiac cause.
        2. unexplained respiratory failure (e.g., not due to fluid overload or acute respiratory distress syndrome [ARDS]), especially if the fibrinogen and/or D-dimer is very high.
        3. Physical findings consistent with thrombosis (superficial thrombophlebitis or retiform purpura not explained by other conditions)

- **Outpatient thromboprophylaxis** (prophylactic dose) may be appropriate in selected individuals with especially high thrombotic risk including prior VTE, recent surgery or trauma, immobilization, or obesity or high IMPROVE score of >2-3. If thromboprophylaxis is used, rivaroxaban 10 mg po od for 35 days is preferred [21]

Table 3 Venous thromboembolic prophylaxis and treatment in patients with COVID-19 disease

	VTE treatment	VTE prophylaxis
Enoxaparin*	**-CrCl ≥30 mL/min:** 1 mg/kg SQ twice daily. **-CrCl (15-30) mL/min:** Reduce to 1 mg/kg OD **-CrCl < 15 contraindicated.** **-BMI ≥40 kg/m^2** a lower dose (i.e., approximately 0.75-1 mg/kg every 12 hours, based on ABW).	**-CrCl ≥30 mL/min:** 40 mg SQ OD **-CrCl (15-29) mL/min:** Reduce to 20 mg SQ OD **-CrCl < 15 contraindicated.** **-BMI 30 to 39 kg/m^2:** 20 mg SQ every 12 hours or 40 mg once daily **-BMI ≥40 kg/m^2** :40 mg every 12 hours).
Heparin	**CrCl < 30 or RRT:** IV heparin (guided by aPTT target protocol). Warfarin is a reasonable PO alternative to use	-BMI ≥50 kg/m^2, 0.6 mg/kg OD **CrCl ≤30** 5,000 units SQ Q8hrs-12hrs

*If patient has history of HIT (Heparin-induced thrombocytopenia) switch to Fondaparinux

	VTE treatment	VTE prophylaxis
Apixaban	10mg PO BID for 7 days then 5mg PO BID	2.5 mg PO bid (regardless of CrCl)
Rivaroxaban	15mg PO BID for 21 days then 20mg daily	10 mg PO OD Avoid Rivaroxaban if CrCl < 30
Fondaparinux	**< 50 kg:** 5 mg SC OD **50-100 kg:** 7.5 mg SC OD >100 kg: 10 mg SC OD CrCl < 30: 50% dose reduction	2.5 mg SC OD **CrCl < 30: 50% dose reduction**

1.3.5 Drugs used in COVID-19 management [5, 6, 10,12]

Table 4 Drugs used in COVID-19 disease management

Medication	Class	Indication/adverse events	Dose and duration	Dose adjustment
Remdesivir[9]	Antiviral	For patients requiring low-flow supplemental oxygen (reduce mortality) Adverse events: nausea, vomiting, and transaminase elevations	Adult (wt > 40 kg): 200 mg IV loading dose on day 1, then 100 mg IV daily maintenance dose. Infuse each dose over 30-120 min. Duration: 5 days if not on ventilation/ECMO. If no clinical improvement at 5 days, extend to 10 days. 10 days for patients on mechanical ventilation/ECMO	Not recommended if eGFR<30 ml/min Discontinue if signs/symptoms of liver inflammation (ALT> 10 times UNL)
Dexamethasone	Anti-inflammatory	For patients on supplemental oxygen or ventilatory support Adverse effects: hyperglycemia, uncontrolled blood pressure and increased risk of infections	6 mg once daily IV or po x 10 days for patients on supplemental oxygen or mechanical ventilation *Equivalent glucocorticoid dose (eg, methylprednisolone 32 mg, prednisone 40 mg) may be substituted if dexamethasone unavailable	No dose adjustment in renal and hepatic impairment
Sotrovimab[8,19,20]	Antiviral (Monoclonal antibody)		Administered as 500 mg IV over 30 minutes (or IM when authorized) Check MOH protocol for identification of possible candidate for Sotrovimab therapy, setting and timing of administration	No dose adjustment in renal and hepatic impairment

1.3.6 Antimicrobial Management of COVID-19 Pneumonia

Tocilizumab	Anti-inflammatory (IL-6 inhibitor)		8 mg/kg, actual body weight up to 800 mg, as a single IV infusion with a second dose 12-24h later if no improvement	No dose adjustment in altered kidney function. Avoid or discontinue in hepatic impairment
Baricitinib[13]	Anti-inflammatory (JAK inhibitor)	Same indications as for Tocilizumab Prophylactic Anticoagulation is highly indicated with JAK inhibitors (risk of thrombosis) Adverse effects: increase risk of infection and rate venous thromboembolism	4 mg orally daily (for 14 days or until discharge, whichever earlier) + Remdesivir 200 mg on day 1, then 100 mg IV daily for up to 10 days ± dexamethasone	requiring renal dose adjustment. Use is not recommended in severe hepatic impairment
Tofacitinib[13]	Anti-inflammatory (JAK inhibitor)		10 mg twice daily (for 14 days or until discharge, whichever earlier)	
Molnupiravir[14] **once approved and authorized in Kuwait**	Oral Antiviral	In non-hospitalized adult patients with COVID-19 who do not require supplemental oxygen, and who are at increased risk of developing severe COVID-19. It should be administered as soon as possible after a diagnosis of COVID-19 and within five days of the onset of symptoms, twice a day for five days	800 mg (four 200 mg capsules) po q12h for five days, with or without food	Not available at present. No renal or hepatic adjustment is required. No known drug-drug interaction
Paxlovid[17]**(Nirmatrelvir and ritonavir) once approved and authorized in Kuwait**	Oral Antiviral	In non-hospitalized adult patients with COVID-19, who are at high risk of progressing to severe illness. It should be administered as soon as possible after a diagnosis of COVID-19 and within five days of the onset of symptoms, twice a day for five days	300 mg (two 150 mg tablets) of nirmatrelvir with one 100 mg tablet of ritonavir, twice-daily for five days	Not available at present. Drug-drug interactions. Require dose adjustment in renal impairment. Use is not recommended in severe hepatic impairment

- Stewardship programs have been shown to optimize antimicrobial use, improve patient outcomes and reduce harms from excess use.
- Bacterial co-infection is relatively infrequent in hospitalized patients with COVID-19. With an admission BAL, potential bacterial pathogen found in 21% of patients[18]
- The majority of COVID-19 patients may not require empirical antibacterial treatment.
- If high suspicion of co-infection or super-infection[12] administer empiric antibiotics within 1 hour of bacterial pneumonia/sepsis suspicion, table 1
- Reevaluate the need to continue antibiotic therapy daily
- Obtain respiratory culture and a MRSA nares screen for all pneumonia cases. Unnecessary antibiotics should be discontinued as soon as possible upon culture maturation, if the clinical status is not deteriorating and/or procalcitonin and WBC are relatively stable

Table 5 Antibiotic algorithm for patients with COVID-19 pneumonia

Pneumonia Severity/ Antibiotic Choice	Option 1 Antibiotic Regimen	Option 2 Antibiotic Regimen	Option 3 Antibiotic Regimen	Option 4 Antibiotic Regimen
Uncomplicated / Colonization	None			
Mild and Moderate pneumonia	Ceftriaxone IV 2g OD + Azithromycin PO 500 mg on day 1 and 250 mg for 4 days	Ceftriaxone IV 2g OD + Doxycycline PO 100 mg BD for 5 days	In penicillin allergic: Moxifloxacin PO 400 mg OD for 5 days Or Levofloxacin PO 750 mg OD for 5 days	
Severe / Critically Ill Patient	Ceftriaxone IV 2g OD +Moxifloxacin 400 mg OD	Ceftriaxone IV 2g OD + Levofloxacin IV 750 mg OD	If positive or highly suspected MRSA, add Teicoplanin (6 mg/kg IV q12 x 3 loading doses: then 6 mg/kg IV q daily) or Linezolid 600mg BD IV/oral to option 1 or 2	Piperacillin/Tazobactam 4.5g IV q6-q8 + Levofloxacin IV 750 mg OD if there is evidence of structural lung disease (e.g., fibrosis bronchiectasis, post-TB destructive lung disease)

*For complicated pneumonia e.g late onset pneumonia after ≥ 5 days in the hospital, risk factors for MDR organisms, with clinical, laboratory or chest radiograph indicating high risk of mortality, we suggest: Meropenem IV 1g TDS or Cefepime 2 g IV TDS) PLUS (Teicoplanin 6mg/kg BD for 3 doses then OD or Linezolid 600 mg IV Bid) PLUS (Levofloxacin 750mg IV OD or Amikacin 15 -20 mg / kg IV OD)

- Dosage should be adjusted according to renal and hepatic function.
- Treat community acquired pneumonia for 5 days only unless complicated pneumonia is proven.
- Reevaluate the need to continue antibiotic therapy daily
- Unnecessary antibiotics should be discontinued as soon as possible upon culture maturation if the clinical status is not deteriorating and/or procalcitonin and WBC are relatively stable.
- Check for multi-drug interaction

1.3.7 Predictor for occurrence of bacterial co-infection:

- Older age
- Co-morbidities
- High WBCs (Neutrophilia and lymphopenia)
- PCT > 0.5
- Low albumin
- Longer hospital duration, Admission to ICU and need for mechanical ventilation
- Corticosteroid use

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Appendix 1 Guidelines for use of Tocilizumab in COVID-19 patients

Guidelines for use of Tocilizumab (Actemra) in COVID-19 patients
Criteria for initiation of Tocilizumab in patients who are at high-risk for developing cytokine storm, must include all the following: • COVID-19 positive • Hospitalized patient • Abnormal chest imaging consistent with COVID-19 • Rapidly worsening gas exchange/respiratory status requiring >4-6 L/min O2 • High clinical suspicion for cytokine release syndrome [16] or systemic inflammation supported by CRP ≥75 mg/L • Benefit probably greatest if administered early within 48h of hospitalization or < 24h after ICU admission
Exclusion Criteria [15] • Active Tuberculosis • Transaminases 5-10 times above reference values (relative) • Active Hepatitis B and Hepatitis C • Neutropenia (<1000 cell/mm3) (relative) • Thrombocytopenia (<50,000 /mm3) • Systemic bacterial or fungal co-infection
Dosing • Doses should be rounded to nearest available full vial (80 mg, 200 mg, 400 mg vials) • Adult Dosing (≥18 years): 8 mg/kg actual body weight up to 800 mg as single IV infusion. With a second dose 12-24 h later if no improvement
*Patients receiving tocilizumab often do not show an immediate response. Improvement generally BEGINS 48-72 hours after administration with cessation of fevers and stabilization or improvement in oxygenation. In the absence of fever, worsening oxygenation alone is not an indication for redosing tocilizumab. It is also important to exclude concomitant bacterial infection when patients do not improve or worsen

Appendix 2 Guidelines for Sotrovimab use in mild-moderate COVID-19 disease

Guidelines for Sotrovimab use in mild-moderate COVID-19 disase
Sotrovimab is recommended for all the following • Mild-to-moderate COVID-19 in adults and pediatric patients (12 years of age and older weighing at least 40 kg) • With positive results of direct SARS-COV-2 viral testing • And who are at high risk for progression to severe COVID-19, including hospitalization or death for administration within 5-10 days of symptom onset as a single intravenous infusion over 30 minutes
High risk is defined as patients who meet at least one of the following criteria: • Older age (for example ≥65 years of age) • Obesity (adults with BMI >35 kg/m2) • Chronic kidney disease • Diabetes • Immunosuppressive disease or immunosuppressive treatment • Cardiovascular disease (including congenital heart disease) or hypertension • Chronic lung diseases (for example, chronic obstructive pulmonary disease, asthma [moderate-to- severe], interstitial lung disease, cystic fibrosis and pulmonary hypertension)

Sotrovimab is not authorized for use in patients: • who are hospitalized due to COVID-19, OR • who require oxygen therapy due to COVID-19, OR • who require an increase in baseline oxygen flow rate due to COVID-19 (in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity)
Dosing • The dose is 500 mg of sotrovimab • It must be diluted and administered as a single intravenous infusion over 30 minutes **Dosage Adjustment in Specific Populations** • No dosage adjustment is recommended based on renal impairment, during pregnancy or while lactating. • No dosage adjustment is recommended in pediatric patients who weigh at least 40 kg and are 12 years of age and older

References

1. https://www.covid19treatmentguidelines.nih.gov/overview/clinical-spectrum
2. Arthur Y Kim, Rajesh T Gandhi. COVID-19: Management in hospitalized adults. Uptodate. https://www.uptodate.com/contents/covid-19-management-in-hospitalized-adults?search=covid&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1. Accessed 15/12/2021
3. https://www.sciencedirect.com/science/article/pii/S1477893920300910?via%3Dihub
4. Clinical Chemistry and Laboratory Medicine (CCLM) (published online ahead of print), 20200198. doi: https://doi.org/10.1515/cclm-2020-0198
5. Gulf health council. GCC Guideline for Screening, Diagnosing and Treatment Of COVID-19. (Version 1.2) June 2021.
6. Ministry of Health, Kuwait. Management recommendations for adults' patients with COVID-19. Nov 2020
7. Acad Emerg Med 2020 Apr 22; [e-pub]. (https://doi.org/10.1111/acem.13994)
8. Early Treatment for Covid-19 with SARS-CoV-2 Neutralizing Antibody Sotrovimab. Gupta A, Gonzalez-Rojas Y, Juarez E, Crespo Casal M, Moya J, Falci DR, Sarkis E, Solis J, Zheng H, Scott N, Cathcart AL, Hebner CM, Sager J, Mogalian E, Tipple C, Peppercorn A, Alexander E, Pang PS, Free A, Brinson C, Aldinger M, Shapiro AE; COMET-ICE Investigators. N Engl J Med. 2021 Nov 18;385(21):1941-1950. doi: 10.1056/NEJMoa2107934.
9. The impact of therapeutics on mortality in hospitalised patients with COVID-19: systematic review and meta-analyses informing the European Respiratory Society living guideline. Crichton ML, Goeminne PC, Tuand K, Vandendriessche T, Tonia T, Roche N, Chalmers JD; European Respiratory Society COVID-19 Task Force.Eur Respir Rev. 2021 Dec 15;30(162):210171. doi: 10.1183/16000617.0171-2021. Print 2021 Dec 31
10. Sandford guide. Management of COVID-19. https://webedition.sanfordguide.com/en/sanford-guide-online/disease-clinical-condition/coronavirus. Accessed on 13/12/2021
11. Pickens CO et al. Bacterial Superinfection Pneumonia in Patients Mechanically Ventilated for COVID-19 Pneumonia. Am J Respir Crit Care Med. 2021 Oct 15;204(8):921-932. doi: 10.1164/rccm.202106-1354OC. PMID: 34409924; PMCID: PMC8534629.
12. NIH. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. https://www.covid19treatmentguidelines.nih.gov. Accessed 12/12/2021
13. NIH, COVID treatment guidelines, The COVID-19 Treatment Guidelines Panel's Statement on Baricitinib for the Treatment of Adults with COVID-19, May 27, 2021, https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-baricitinib/)
14. William Fischer at al, Molnupiravir, an Oral Antiviral Treatment for COVID-19, medRxiv, 10.1101/2021.06.17.21258639
15. Adopted from https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html
16. Adopted from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7270045/
17. Covid-19: Pfizer's paxlovid is 89% effective in patients at risk of serious illness, company reports. Mahase E.BMJ. 2021 Nov 8;375:n2713. doi: 10.1136/bmj.n2713.
18. He S, et al. Clinical characteristics of COVID-19 patients with clinically diagnosed bacterial co-infection: A multi-center study. PLoS One. 2021 Apr 5;16(4):e0249668. doi: 10.1371/journal.pone.0249668. PMID: 33819304; PMCID: PMC8021165.
19. CDC. People with certain medical conditions. https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html. Accessed 13/12/2021
20. Early Treatment for Covid-19 with SARS-CoV-2 Neutralizing Antibody Sotrovimab. Anil Gupta, M.D., Yaneicy Gonzalez-Rojas, M.D., Erick Juarez, M.D., Manuel Crespo Casal, M.D., Jaynier Moya, M.D., Diego R. Falci, M.D., Ph.D., Elias Sarkis, M.D., Joel Solis, M.D., Hanzhe Zheng, Ph.D., Nicola Scott, M.Sc., Andrea L. Cathcart, Ph.D., Christy M. Hebner, Ph.D., et al., for the COMET-ICE Investigators· N Engl J Med 2021; 385:1941-1950. DOI: 10.1056/NEJMoa2107934
21. Rivaroxaban versus no anticoagulation for post-discharge thromboprophylaxis after hospitalization for COVID-19 (MICHELLE): an open-label, multicentre, randomised, controlled trial Ramacciotti, Eduardo Benevenuto Caltabiano, Tania et al. The Lancet, Volume 399, Issue 10319, 50 - 59

22. Thromb Haemost 2020 Mar 25; [e-pub]. (https://doi.org/10.1111/JTH.14810)
23. ATTACC Investigators; ACTIV-4a Investigators; REMAP-CAP. Therapeutic Anticoagulation with Heparin in Noncritically Ill Patients with Covid-19. N Engl J Med. 2021 Aug 26;385(9):790-802. doi: 10.1056/NEJMoa2105911. Epub 2021 Aug 4. PMID: 34351721; PMCID: PMC8362594.
24. Sholzberg M, Tang G H, Rahhal H, AlHamzah M, Kreuziger L B, Ã□inle F N et al. Effectiveness of therapeutic heparin versus prophylactic heparin on death, mechanical ventilation, or intensive care unit admission in moderately ill patients with covid-19 admitted to hospital: RAPID randomised clinical trial BMJ 2021; 375 :n2400 doi:10.1136/bmj.n2400
25. Spyropoulos AC, Goldin M, Giannis D, et al. Efficacy and Safety of Therapeutic-Dose Heparin vs Standard Prophylactic or Intermediate-Dose Heparins for Thromboprophylaxis in High-risk Hospitalized Patients With COVID-19: The HEP-COVID Randomized Clinical Trial. JAMA Intern Med. 2021;181(12):1612–1620. doi:10.1001/jamainternmed.2021.6203