Croydon Health Services NHS
NHS Trust

Title	Protocol for the management of COVID-19 in the non-critical care setting
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1. Introduction

December 2019 witnessed the emergence of a novel and highly contagious coronavirus, severe adult respiratory syndrome coronavirus 2 (SARS-CoV-2), causing Coronavirus Disease 2019 (COVID-19). It spread rapidly from the first outbreak in Wuhan, China, and was declared a pandemic on March 11th 2020. Clinical presentation can range hugely in severity, with the predominant presentation of significant illness being respiratory in nature. However, it is clear that COVID-19 infection can be a multisystem disease with respiratory, renal, cardiovascular, haematological, dermatological and neuropsychological sequelae.

To date, there have been hundreds of thousands of infections in the UK, with the initial peak in infections occurring between March and May 2020. After a period of suppression of the virus following the national lockdown and other social distancing measures, and as we move into the autumn and winter months of 2020, case numbers are again rising, as expected. This protocol document outlines the management of severe COVID-19 disease. Clinicians will need to manage possible COVID-19 disease alongside other respiratory infections common during winter, such as influenza and community acquired pneumonia, which can be indistinguishable. Patients with severe disease will require admission to hospital for oxygen therapy as well as other interventions, such as careful fluid management and thromboprophylaxis, based on the knowledge base to date.

2. Clinical presentation

Common symptoms:

Fever, breathlessness, persistent dry cough, loss of taste/smell, myalgia
GI disturbance
Chest pain

Severe Covid-19 in adults is defined as:

- Dyspnea
- Respiratory rate > 30 or more breaths per minute
- Blood oxygen saturation of 93% or less
- Ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen (PaO2:FiO2) < 300 mm Hg
- Infiltrates in > 50% of the lung field within 24 to 48 hours from the onset of symptoms

Patients are typically most infectious 1-2 days prior to the onset of symptoms and up to 7 days after. Following exposure, if no symptoms are present up to 14 days (incubation period), then they are unlikely to develop after this period, hence the quarantine duration. Asymptomatic transmission is a key phenomenon of this disease.

Disease phases:

1. Early or viral response phase – mainly upper respiratory tract symptoms
2. Pulmonary phase – pneumonia
3. Hyper inflammation phase – ARDS, multi-organ involvement

Criteria for admission:

Saturation <92% on air OR sats 93-94% with significant desaturation on exertion (>3% from resting sats)

Tachypnoea (RR>20)
Haemodynamic instability

Investigations:

CXR – peripheral ground glass opacities/consolidation
Bloods – FBC (lymphopenia), U&E, LFTs, CRP, CK, trop, D-dimer, ABG, ferritin
Nasal swab for RT-PCR antigen test
Atypical pneumonia screen (legionella and pneumococcal antigen, mycoplasma serology)

These tests must be performed on admission. For further details please see Appendix 1.

In addition:
CTPA if concern for pulmonary embolism (PE)
CT chest if diagnostic uncertainty (i.e. clinical features but negative SARS-CoV-2 PCR)
CT brain if neurological symptoms
Repeat CXR & blood tests in case of clinical change

Treatment escalation plans

It is essential that TEP and DNAR status as well as ceilings of care are discussed early with patients at time of admission. Use of Rockwood clinical frailty score is helpful in making these decisions (which should be done by senior clinicians). Co-morbidities (both severity and number) should also be clarified. Collateral history is critical if patient unable to give history. If uncertain, second opinion from consultants (including respiratory and co-ordinating on call critical care) can be sought. Challenging cases can be referred to MAG (Medical Advisory Group) who are available out of hours.

Escalation of treatment

If patients are suitable for escalation of treatment to either HFNO/CPAP or invasive mechanical ventilation (IMV), liaise with CCOT and Respiratory/Critical Care consultant regarding this.
(Appendix 1).

3. Infection control considerations

COVID-19 is highly infectious and patients should be isolated to prevent cross infection to other patients and staff.

1. Personal Protective Equipment (PPE)

For the up to date PPE guidance please follow the link below:

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/910885/COVID-19_Infection_prevention_and_control_guidance_FINAL_PDF_20082020.pdf

All staff are reminded to wear the appropriate PPE at all times for the specific tasks

Aerosol-generating procedures (AGPs):

AGPs include;

- Intubation, extubation and related procedures, for example - open suctioning of the respiratory tract
- Bronchoscopy and upper ENT airway procedures that involve suctioning
- Upper gastro-intestinal endoscopy where there is open suctioning of the upper respiratory tract
- Surgery and post mortem procedures involving high-speed devices high speed cutting in surgery/post mortem procedures if this involves the respiratory tract or paranasal sinuses
- Some dental procedures (for example, high-speed drilling)
- Non-invasive ventilation (NIV); Bi-level Positive Airway Pressure Ventilation (BiPAP) and Continuous Positive Airway Pressure Ventilation (CPAP)
- High Frequency Oscillatory Ventilation (HFOV)
- Induction of sputum
- High flow nasal oxygen (HFNO)
- Cardiology TOE
- Cardio Pulmonary Resuscitation (CPR)

Please note that staff do not need to self-isolate after delivering care to COVID-19 positive patients. Wearing of PPE offers protection and removes the need for self-isolation.
Please maintain safe social distancing while on breaks and good hand hygiene to keep safe.

2. Patient flow

Low case numbers – patients with suspected or confirmed disease (from prior swab in hospital/community) to be isolated in side rooms in ED and then to side rooms on wards.

High case numbers – patients to be cohorted into confirmed and suspected bays on designated COVID wards. Decision to triage patients to COVID ward is a senior clinical decision by registrar or consultant in conjunction with the site team (needs to be clearly documented on CERNER by medical registrar as low or high risk for COVID-19). *Patients should not be moved from ED until this process has been followed.*

Patienteer is the primary tool used to manage the flow and safe allocation of beds within Croydon Hospital. The real-time capabilities of the system also allow for the quick detection of deteriorating patients with suspected and confirmed Covid-19.

Based on the data entered in eMR the system has many rules and smarts that instantaneously provide a Covid-19 status for each patient, which are amended or confirmed by the site team.

Within the tool each bed is coloured to represent a certain status:

Yellow: Not Suspected
Orange: Suspected
Green: Negative
Purple: Exposed
Red: Positive

Patienteer tracks the Covid-19 swab journey in real-time, allowing for the user to “at a glance” identify and address delays within the workflow.

4. Treatment considerations

There is no cure for COVID-19 and treatment to date has been supportive. Numerous trials are in progress and CUH is participating in many. Trials offer further treatment options which would not otherwise be available to patients.

1. Supplemental oxygen, HFNO & CPAP

Both HFNO and CPAP generate significant aerosol so should be administered in side room, ideally with negative pressure ventilation to minimise risk of cross infection of other patients/staff. However, as case numbers increase, cohort bays for CPAP/HFNO will be used.

- CPAP to be vetted by duty respiratory consultant
- Daily MDT with CCOT, ICU and Respiratory to review CPAP/HFNO patients.

2. Steroids

As per outcome of RECOVERY trial reported in June 2020 – 20% reduction in mortality in patients requiring supplemental oxygen; 33% reduction in mortality in ventilated patients receiving Dexamethasone 6mg od; no benefit in those not needing oxygen

Give dexamethasone 6 mg OD for 10 days or until discharge (whichever is soonest).

(Alternative corticosteroids (Prednisolone, Hydrocortisone, Methlyprednisolone) can be used if Dexamethasone not available but equivalence of effect not tested in trial).

3. Remdesivir

Remdesivir is an adenosine nucleotide prodrug. It inhibits SARS-CoV-2 RNA polymerase.
Eligibility:

- For patients who require supplemental oxygen. (Not requiring oxygen delivery through a High-Flow Device, Non Invasive Ventilation, Invasive Mechanical Ventilation, or ECMO). If a patient who is on supplemental oxygen while receiving Remdesivir progresses to requiring delivery of oxygen through a high-flow device, non-invasive ventilation, invasive mechanical ventilation, or ECMO, the course of Remdesivir should be completed.
- Adults, adolescents ≥ 12 years of age and ≥ 40 kg,
- eGFR ≥ 30ml/min, ALT below 5 times the upper limit of normal at baseline. Remdesivir for 5 days or until hospital discharge, whichever comes first (see Appendix).
- Discontinue in patients who develop ALT ≥ 5, ALT elevation accompanied by signs or symptoms of liver inflammation.

4. Treatments available through clinical trials:

i) **Recruit to RECOVERY Trial**. Inclusion criteria - in hospitalised patients with no medical history that might in the opinion of the attending clinician, put the patient at significant risk if he/she were to participate in this aspect of the RECOVERY trial. First randomisation to no additional treatment vs convalescent plasma. Second randomisation (if worsening symptoms and signs) to no additional treatment vs Tocilizumab. Contact Dr Teresa Costello or Dr Sundar Raj Ashok for advice.

- **Convalescent plasma:** Single unit of ABO compatible convalescent plasma (275mls +/- 75 mls) intravenous per day on study days 1 (as soon as possible after randomisation) and 2 (with a minimum of 12-hour interval between 1st and 2nd units).
  Convalescent plasma COVID-19 FFP (CP) is plasma donated from patients who have recovered from COVID-19 and contains antibodies which may neutralise SARS-CoV-2 virus. Adult dose: One unit (275 ± 75 mL) on days 1 and 2. BEFORE convalescent plasma can be supplied by transfusion lab two group & screen samples must have been sent to laboratory (taken at separate times), assess for potential transfusion associated circulatory overload, antibody-dependent enhancement (theoretically antibodies may promote viral entry into cells and accelerate disease. No clear evidence of this in humans), DURING transfusion watch for hypersensitivity reaction to plasma

- **Tocilizumab**. Humanized monoclonal antibody against IL-6 receptor. Inclusion criteria: Randomised into the RECOVERY trial no more than 21 days ago, clinical evidence of progressive COVID-19: a) oxygen saturation <92% on room air or requiring oxygen, b) C-reactive protein ≥75 mg/L, clear evidence to exclude secondary bacterial infection causing deterioration. Do not initiate if absolute neutrophil count less than 2 x 109/litre, severe active infection. Discontinue if absolute neutrophil count less than 0.5 x 109/litre or platelet count less than 50 x 103/microliter. Caution if hepatic enzymes more than 1.5 times the upper limit of normal. Discontinue if hepatic enzymes more than 5 times the upper limit of normal.

ii) **Recruit to REMAP CAP trial.** For patients transferred straight into ITU. Randomisation to no immunoglobulin vs convalescent plasma. Please contact Dr Taha Othmane, Dr Nabil Nizar, Dr Ajikumar Kavidasan or Dr Sundar Raj Ashok for advice.

- Convalescent plasma: Inclusion criteria: Within 48 hours of ITU admission, patient has not received treatment with any non-trial prescribed antibody therapy (monoclonal antibody, hyperimmune immunoglobulin, or convalescent plasma) intended to be active against COVID-19 during this hospital admission, within 14 days of hospital admission.
- One and not more than two adult units of ABO compatible convalescent plasma (total volume 550ml ± 150ml) within 48 hours of randomization.

Note no evidence for efficacy of Hydroxychloroquine
No evidence for of antiviral/IL-6 antagonist outside clinical trial

5. Anticoagulation

Please note there are some amendments to the full policy available on the Trust intranet. Further changes will be made after London guidelines are published in the next few weeks.

Higher incidence of venous and arterial thrombosis due to inflammatory response to SARS-CoV-2 (PE, stroke)

- **Determining the type and dose of prophylactic anticoagulation:**

Inclusion Criteria for intermediate thromboprophylaxis:

 Confirmed Covid-19 from antigen swab testing

 Suspected Covid-19 (classic history OR classic CXR changes OR raised fibrinogen + D-Dimer + Ferritin + LDH)

Exclusion criteria:

 Age <16 years

 Pregnancy

 High risk bleeding risk factors (see Table 1 below). If any of the bleeding risk factors are met, please consider discussing with a haematologist to individualise a thromboprophylaxis plan.

Table 1: Bleeding risk factors

- Active bleeding *
- Thrombocytopenia (platelet count <50 x 10^9/L)^^
- Fibrinogen <1.5g/L
- Concurrent use of anticoagulants such as warfarin with INR > 2 or DOAC
- Acute stroke†
- Uncontrolled systolic hypertension (> 230/120 mmHg)
- Untreated inherited bleeding disorders (such as haemophilia)
- Acquired bleeding disorders eg. Acquired haemophilia
- Trauma patients #
- Recent critical site surgery eg. Neurosurgery, spinal surgery or eye surgery
- Lumbar puncture/epidural/spinal anaesthesia within the previous 4 hours or expected within the next 12 hours
- Other procedures with high bleeding risk #

Defined as one of the following
i. unexplained drop in Hb of >20g/L
ii. unexplained haemodynamic instability though possibly due to bleeding
iii. macroscopic haemorrhage eg. Haematemesis, maleana, haematuria, epistaxis etc
^^If platelets 30-50x109 /L, consider standard dose LMWH prophylaxis in the absence of additional bleeding risk factors and monitor platelet count daily
† If acute stroke occurs and mechanical prophylaxis is contraindicated, consider pharmacological prophylaxis daily in the MDT
# Review the bleeding risk daily in the MDT and consider escalating to intermediate dose anticoagulant prophylaxis as soon as appropriate

For all patients with high bleeding risk, apply mechanical prophylaxis unless contraindicated (see Table 2 below), with individual decision to add standard LMWH thromboprophylaxis as per Trust guidelines. Discussion with a haematologist is recommended.

Table 2: Contraindications to mechanical prophylaxis

- Lower limb ischaemia and suspected or proven peripheral vascular disease
- Peripheral arterial bypass grafting or vein harvest for CABG
- Peripheral neuropathy or other cause of sensory impairment
- Recently diagnosed lower limb DVT (do not use SCD if DVT within last 4 weeks)
- Allergy to material of manufacture
- Severe leg oedema
- Local condition in which compression may cause damage (e.g. fragile tissue paper skin, dermatitis, gangrene, recent skin graft)
- Unusual leg size or shape, or major limb deformity
- Severe right sided cardiac failure

- **Patients taking Direct oral anticoagulants (DOACs) or Vitamin K antagonists (such as Warfarin)**

Antibiotics and antiviral drugs can have significant drug-drug interactions with all classes of anticoagulant agents. Moreover there could be issues with oral intake or impaired GI absorption. In such cases, consider switching to subcutaneous LMWH in patients taking DOACs or Vitamin K antagonists (such as Warfarin) for stroke prevention in atrial fibrillation or for previous VTE. Oral anticoagulation can be resumed when clinically appropriate.
Patients with a metallic heart valve or established on warfarin with an INR target of 3-4 should be discussed with a haematologist. Dalteparin with anti-Xa monitoring (with a target of 1-2 units/mL) may be recommended.

- **For all patients with low bleeding risk:**

 Obtain the ACTUAL BODY WEIGHT

 Calculate the most recent Creatinine clearance using the Cockcroft Gault equation

 Determine the dose of intermediate thromboprophylaxis using Table 3 below:

Table 3: Intermediate thromboprophylaxis for patients with suspected/confirmed Covid-19 infection

Weight (kg)	Creatinine Clearance	
	>30mls/min	<30mls/min or on RRT
<45kg	5,000 units OD Dalteparin s/c	2,500 units OD Dalteparin s/c
45-99kg	5,000 units BD Dalteparin s/c	5,000 units OD Dalteparin s/c
100-149kg	7,500 units BD Dalteparin s/c	7,500 units OD Dalteparin s/c
>150kg	10,000 units BD Dalteparin s/c	5,000 units BD Dalteparin s/c

Perform anti-Xa level for patients with a CrCl <20mls/min or on RRT. Anti-Xa blood sample must be taken 4 hours after ≥3rd dose of Dalteparin. Aim for anti-Xa level of 0.3-0.7 units/ml.

- **Patients with a high suspicion of VTE**

 Diagnosis of VTE should be made using standard methods including Doppler and CTPA based on clinical suspicion and risk assessment.

 Routine screening for VTE is not advised.

 Do not use treatment dose dalteparin or heparin infusion for primary prevention unless part of a clinical trial

 Offer 3 months of therapeutic dose anticoagulation to all patients with a high suspicion/confirmed VTE.

Table 4: Therapeutic dose dalteparin dosing schedule

Weight	CrCl >30mls/min	*CrCl 20-30mls/min or on RRT or platelets <50 x10^9/L#	*Cr Cl <20mls/min
<45kg	7,500 units OD	5,000 units OD	5,000 units OD
45-56kg	10,000 units OD	7,500 units OD	5,000 units OD
57-68kg	12,500 units OD	10,000 units OD	7,500 units OD
69-82kg	15,000 units OD	12,500 units OD	7,500 units OD
83-100kg	18,000 units OD	12,500 units OD	10,000 units OD
101-115kg	10,000 units BD	15,000 units OD	10,000 units OD
116-140kg	12,500 units BD	18,000 units OD	12,500 units OD
>140kg	15,000 units BD	10,000 units AM AND 12,500 units PM	15,000 units OD

***Check anti-Xa level for patients with a CrCl <30mls/min or on RRT – sample should be obtained 4 hours post dose, with a target level of 0.5-1.0 units/ml**
 # Consider split dose dalteparin to avoid high peaks of dalteparin levels. If the dalteparin dose is split, aim for anti Xa level of 0.5-0.8 units/ml.

- **Patients unable to have heparin derivatives**

Non heparin anticoagulants should be used in the following groups of patients:
 History of heparin induced thrombocytopenia (HIT)

 Currently suspected or confirmed HIT

 Known allergy to heparin, dalteparin or porcine products

 Patients unable or unwilling to have products of animal origin for any reason

Table 5 : Non heparin anticoagulation for patients with suspected/confirmed Covid-19 infection

Creatinine clearance	INTERMEDIATE DOSE THROMBOPROPHYLAXIS	THERAPEUTIC ANTICOAGULATION
>20 ml/min	Fondaparinux 2.5mg BD S/C	<50kg: Fondaparinux 5mg OD S/C 51-100kg: Fondaparinux 7.5mg OD S/C >100kg: Fondaparinux 10mg OD S/C
Below 20 ml/min or on RRT	ARGATROBAN INFUSION- REFER TO PROTOCOL BELOW	

Performing anti-Xa level is advisable in renal impairment. Anti-Xa blood sample must be taken 4 hours after >3rd dose of fondaparinux. Aim for anti-Xa level of 0.3-0.7 units/mL for patients on intermediate thromboprophylaxis and 0.5-1 units/mL for patients on therapeutic anticoagulation.

For Argobatran and Intensive Care protocol please see main guideline document on Trust Intranet

6. Renal impairment

Likely multifactorial – high insensible losses due to respiratory failure, high fever; direct inflammatory effect; microvascular thrombi. Patients presenting with hypoxia likely to be fluid deplete due to being unwell for several days prior to attending hospital.
Careful fluid management with rehydration, taking into account replacement of losses:

- Fluid boluses on admission to restore hypovolaemia - aim for at least +1L (or 10ml/kg) in acute phases given the high insensible losses with high Resp Rate
- Weight determined fluid management (not 8hrly etc) - 1ml/kg/hr minimum input, as per NICE
- Patients on CPAP should be catheterised and accurate fluid balance kept
- Clinical and biochemical observations of hypovolaemia - Cap refiill, peripheral temperature, thirst, urea - trigger for fluid bolus

7. Cardiac

Echocardiogram if significant cardiac enzymes/haemodynamic instability/arrhythmia

8. Neurological

Low threshold for CT imaging if delirium or new neurological deficit in view of known risk of stroke

9. Nutritional

Difficulty maintaining nutrition during high catabolic state, or if high respiratory rate; especially if needing NIV
Routine use of nutritional supplements and consider early NG feeding if unable to maintain intake (risk vs benefit needs to weighed up in each case if on NIV)

10. Vitamin D

70% of UHL inpatients with COVID who had a Vitamin D level measured had low levels. A recent Spanish RCT of 76 patients suggests acute Vitamin D supplementation at high dose in hospitalised patients with COVID reduces admission to ITU and severe outcomes. As a minimum please measure Vitamin D levels and supplement if low: Dosing – 40000 units daily for 1 week protocol for deficiency, and a daily 800-1000iu if sufficient.

11. Antibiotics

Rationalise use; if no suspected bacterial co-infection, no evidence for benefit of use of empirical antibiotic treatment for bacterial pneumonia. If suspected bacterial pneumonia refer to Trust antibiotics guidelines (Appendix 2). Consider routine use of procalcitonin to differentiate bacterial vs viral infection, and as a trigger to de-escalate antibiotic treatment

12. COVID-19 clinic – post COVID/long COVID

Recovery can range from 1-2 weeks to months, depending on disease severity. Cough and fatigue are most likely to persist though occasionally fevers and chills may. Older patients with great comorbidities may take longer to return to baseline. There is emerging data for ongoing respiratory impairment, cardiac sequelae and post intensive care syndrome (cognition, mental and physical impairment).

Follow up on discharge for all patients with confirmed COVID-19 (to be added on discharge letter and ward clerks to book the appointment). Guidelines for follow up on Intranet.

5. References

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6. Appendices

Appendix 1: Summary of management of severe COVID-19 infection

Criteria for admission:

- Saturation <92% on air OR sats 93-94% with significant desaturation on exertion (>3% from resting sats)
- Tachypnoea (RR>20)
- Haemodynamic instability

Investigations:

- CXR – peripheral ground glass opacities/consolidation
- Bloods – FBC (lymphopenia), U&E, LFTs, CRP, CK, trop, D-dimer, ABG, ferritin
- Nasal swab for RT-PCR antigen test
- Atypical pneumonia screen (legionella and pneumococcal antigen, mycoplasma serology)

Ensure TEP and escalation plan set on admission

Treatment:

- Supplemental O2/HFNO/CPAP
  Dexamethasone 6 mg OD for 10 days or until discharge (whichever is soonest) for patients with severe COVID-19 pneumonia needing steroids.
- Remdesivir for 5 days or until hospital discharge, whichever comes first
- Anticoagulation - If D-Dimer is above1800 ng/mL, consider therapeutic dose anticoagulation if there are no bleeding risk factors
- Consider trial recruitment
- IV fluids
- Vitamin D supplementation
- Antibiotics if concurrent bacterial infection

Appendix 2: Laboratory and microbiological testing

Laboratory features associated with severe COVID-19

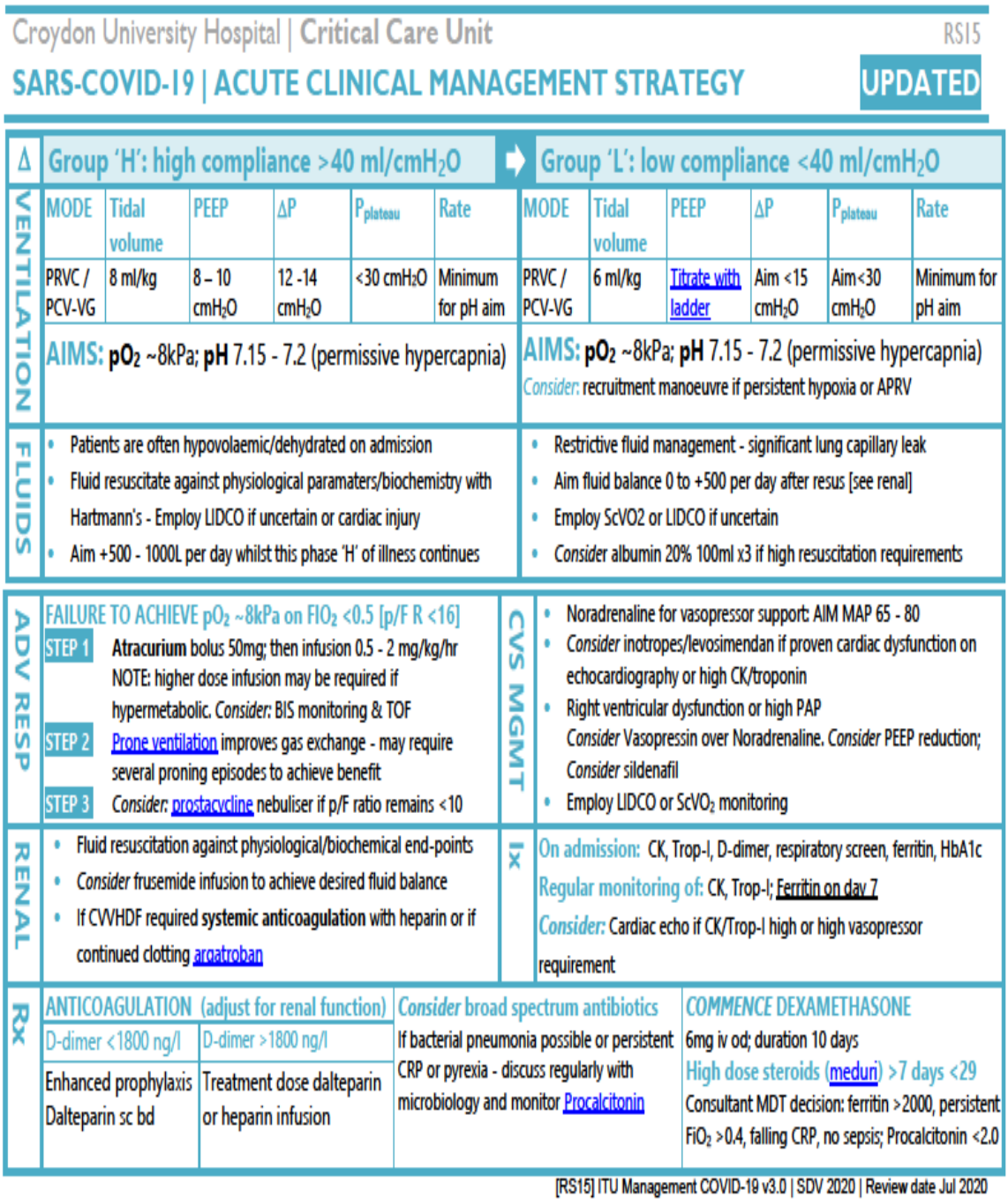
Abnormality	Possible threshold
Elevations in:	
▪ D-dimer	>1000 ng/mL (normal range: <500 ng/mL)
▪ CRP	>100 mg/L (normal range: <8.0 mg/L)
▪ LDH	>245 units/L (normal range: 110 to 210 units/L)
▪ Troponin	>2× the upper limit of normal (normal range for troponin T high sensitivity: females 0 to 9 ng/L; males 0 to 14 ng/L)
▪ Ferritin	>500 mcg/L (normal range: females 10 to 200 mcg/L; males 30 to 300 mcg/L)
▪ CPK	>2× the upper limit of normal (normal range: 40 to 150 units/L)
Decrease in:	
▪ Absolute lymphocyte count	<800/microL (normal range for age ≥21 years: 1800 to 7700/microL)

Microbiology testing:

- Nasal swab RT-PCR is the test of choice for acute COVID – single bagged, brought to laboratory in red box by porter, processed at South West London Pathology, St George's Hospital. Turn-around time: 24-48 hrs
- If negative and high index of suspicion/infection control risk implications, then please send repeat test
- Indeterminate results should be managed as positive in the context of a high clinical index of suspicion/given the specificity of PCR tests
- Lower respiratory tract specimens offer greater sensitivity than nasal swab but require microbiology approval e.g. severely unwell patients where there is diagnostic uncertainty after a negative swab
- Urgent PCR testing is available for selected patients on discussion with microbiology. Turn-around time: 1 hour. Appropriate scenarios for this include severe infection/requiring ITU admission, urgent transfers to other hospitals for emergency care where acceptance is contingent on a COVID swab result, outbreak management as directed by the infection control team – please discuss with microbiology if urgent testing required.
- Due to COVID workload, extended viral respiratory PCR (Influenza A/B, RSV, Mycoplasma, Rhinovirus, other coronaviruses etc.) is not being routinely processed but is available on consultant microbiologist request on clinical grounds. Rapid flu A/B/RSV testing will be available in due course follow later in the season.

- Serology is not appropriate for the diagnosis of acute COVID, does not reliably predict immunity and may wane with time but can identify patients who have previously had COVID.

Appendix 3: ITU guidelines for COVID-19 Management



Croydon University Hospital | Critical Care Unit — RS15

SARS-COVID-19 | ACUTE CLINICAL MANAGEMENT STRATEGY — UPDATED

Δ VENTILATION

Group 'H': high compliance >40 ml/cmH2O						Group 'L': low compliance <40 ml/cmH2O					
MODE	Tidal volume	PEEP	ΔP	$P_{plateau}$	Rate	MODE	Tidal volume	PEEP	ΔP	$P_{plateau}$	Rate
PRVC / PCV-VG	8 ml/kg	8 – 10 cmH2O	12 -14 cmH2O	<30 cmH2O	Minimum for pH aim	PRVC / PCV-VG	6 ml/kg	Titrate with ladder	Aim <15 cmH2O	Aim<30 cmH2O	Minimum for pH aim
AIMS: **pO2** ~8kPa; **pH** 7.15 - 7.2 (permissive hypercapnia)						AIMS: **pO2** ~8kPa; **pH** 7.15 - 7.2 (permissive hypercapnia) *Consider:* recruitment manoeuvre if persistent hypoxia or APRV					

FLUIDS

- Patients are often hypovolaemic/dehydrated on admission
- Fluid resuscitate against physiological paramaters/biochemistry with Hartmann's - Employ LIDCO if uncertain or cardiac injury
- Aim +500 - 1000L per day whilst this phase 'H' of illness continues

- Restrictive fluid management - significant lung capillary leak
- Aim fluid balance 0 to +500 per day after resus [see renal]
- Employ ScVO2 or LIDCO if uncertain
- *Consider* albumin 20% 100ml x3 if high resuscitation requirements

ADV RESP

FAILURE TO ACHIEVE pO_2 ~8kPa on FIO_2 <0.5 [p/F R <16]

STEP 1 **Atracurium** bolus 50mg; then infusion 0.5 - 2 mg/kg/hr NOTE: higher dose infusion may be required if hypermetabolic. *Consider:* BIS monitoring & TOF

STEP 2 Prone ventilation improves gas exchange - may require several proning episodes to achieve benefit

STEP 3 *Consider:* prostacyclin nebuliser if p/F ratio remains <10

CVS MGMT

- Noradrenaline for vasopressor support: AIM MAP 65 - 80
- *Consider* inotropes/levosimendan if proven cardiac dysfunction on echocardiography or high CK/troponin
- Right ventricular dysfunction or high PAP *Consider* Vasopressin over Noradrenaline. *Consider* PEEP reduction; *Consider* sildenafil
- Employ LIDCO or $ScVO_2$ monitoring

RENAL

- Fluid resuscitation against physiological/biochemical end-points
- *Consider* frusemide infusion to achieve desired fluid balance
- If CVVHDF required **systemic anticoagulation** with heparin or if continued clotting argatroban

Ix

On admission: CK, Trop-I, D-dimer, respiratory screen, ferritin, HbA1c

Regular monitoring of: CK, Trop-I; Ferritin on day 7

Consider: Cardiac echo if CK/Trop-I high or high vasopressor requirement

Rx

ANTICOAGULATION (adjust for renal function)	
D-dimer <1800 ng/l	D-dimer >1800 ng/l
Enhanced prophylaxis Dalteparin sc bd	Treatment dose dalteparin or heparin infusion

Consider broad spectrum antibiotics

If bacterial pneumonia possible or persistent CRP or pyrexia - discuss regularly with microbiology and monitor Procalcitonin

COMMENCE DEXAMETHASONE

6mg iv od; duration 10 days

High dose steroids (meduri) >7 days <29

Consultant MDT decision: ferritin >2000, persistent FiO_2 >0.4, falling CRP, no sepsis; Procalcitonin <2.0

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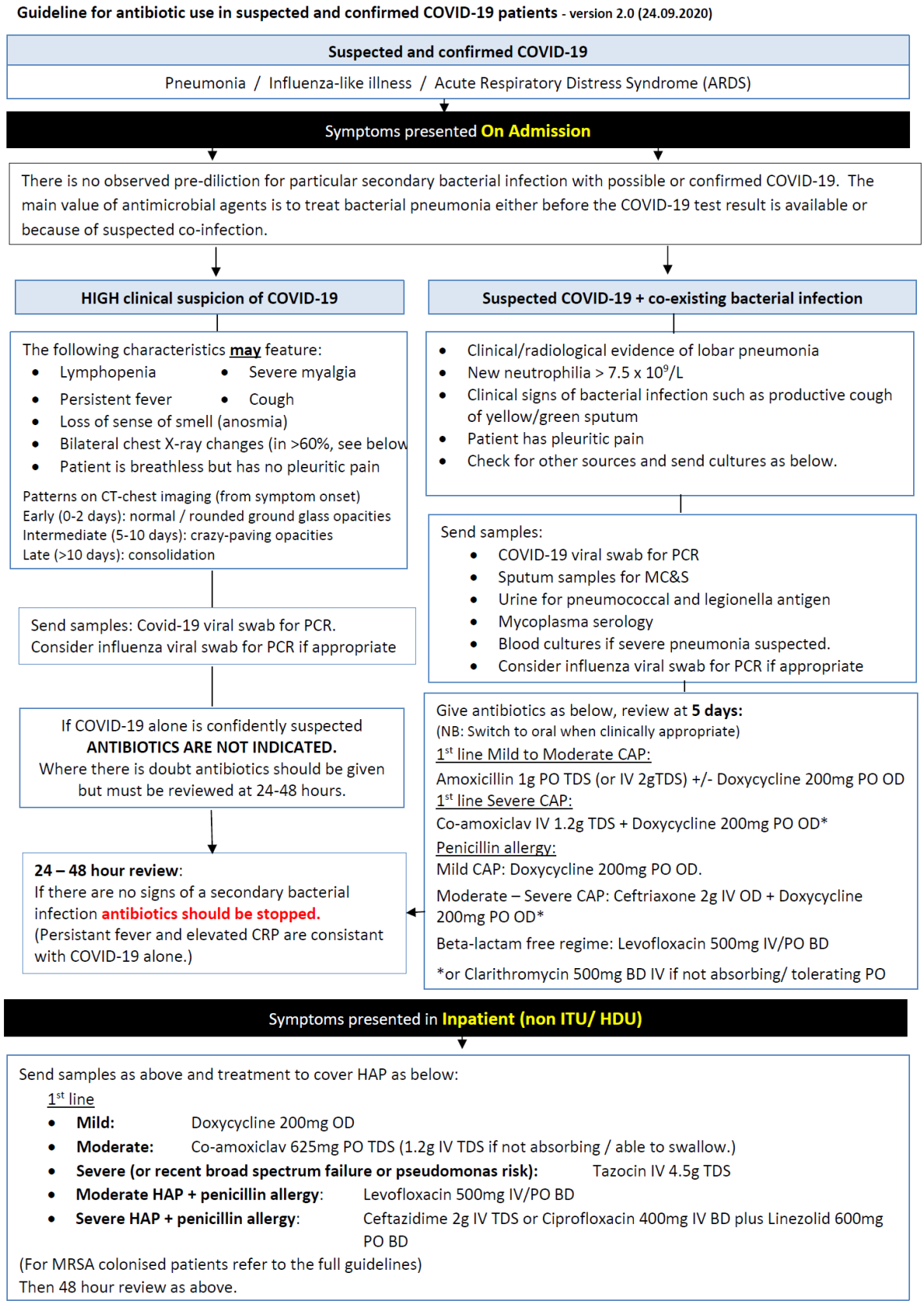
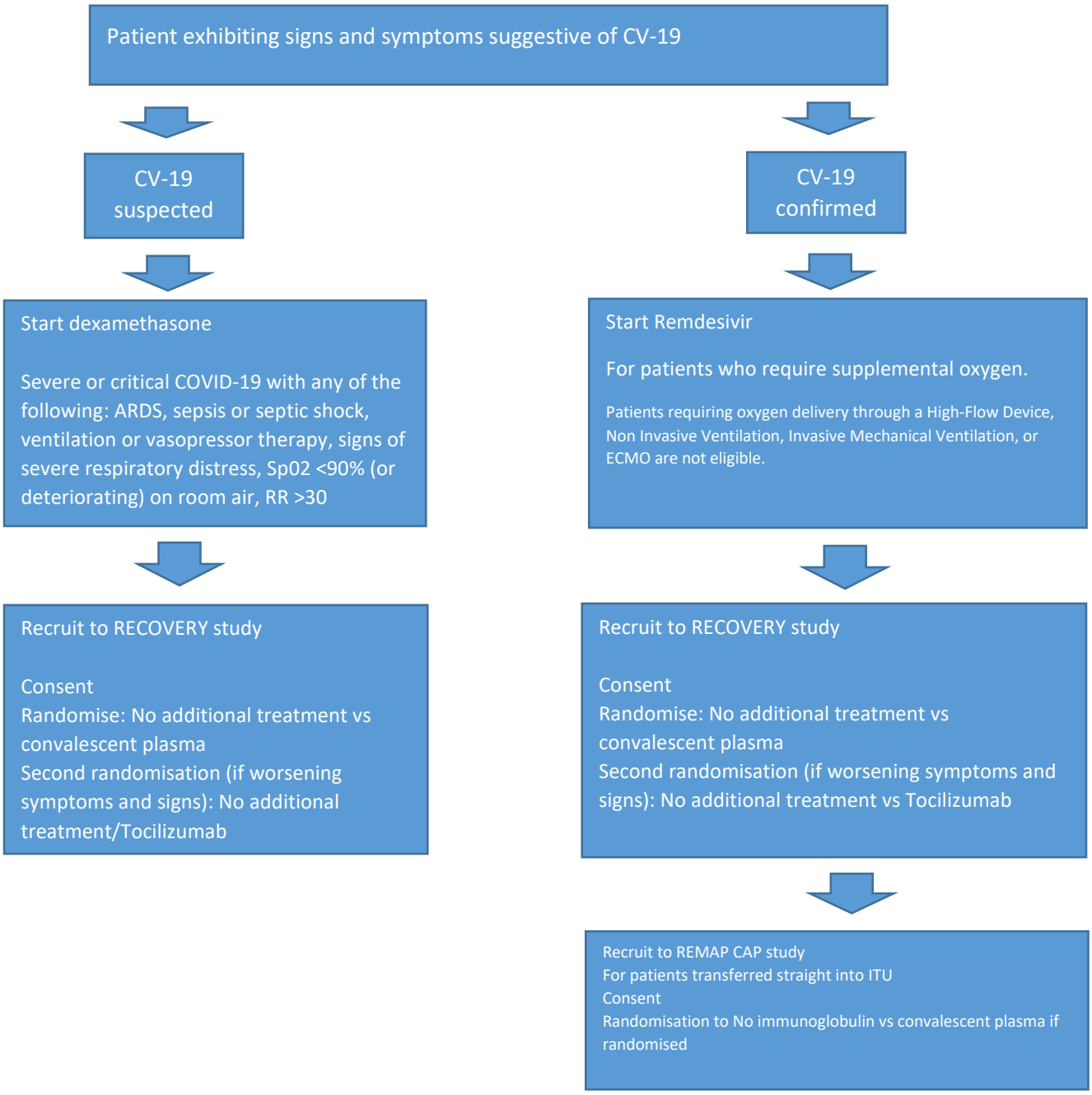
Appendix 4: Antibiotics Guidelines for COVID-19



Appendix 5 – Clinical trials flowchart



Convalescent plasma COVID-19 FFP (CP) is plasma donated from patients who have recovered from COVID-19 and contains antibodies which may neutralise SARS-CoV-2 virus.
Adult dose: One unit (275 ± 75 mL) on days 1 and 2

- Administered at least 12 hours apart
- Administer as soon as possible and within 4 hours of defrosting if at room temperature or up to 24 hours if refrigerated between 2 - 6°C

BEFORE convalescent plasma can be supplied by transfusion lab two group & screen samples must have been sent to laboratory (taken at separate times)
BEFORE administering convalescent plasma

- Assess for potential transfusion associated circulatory overload
- Antibody-dependent enhancement. Theoretically antibodies may promote viral entry into cells and accelerate disease. No clear evidence of this in humans

DURING Watch for hypersensitivity reaction to plasma

Tocilizumab. Humanized monoclonal antibody against IL-6 receptor. Eligibility criteria:

- Receiving oxygen or oxygen saturations <92% on air
- CRP ≥75 mg/L
- Clear evidence to exclude secondary bacterial infection causing deterioration

Do not initiate if absolute neutrophil count less than 2 x 109/litre, severe active infection
Discontinue if absolute neutrophil count less than 0.5 x 109/litre or platelet count less than 50 x 103/microlitre.
Caution if hepatic enzymes more than 1.5 times the upper limit of normal. Discontinue if hepatic enzymes more than 5 times the upper limit of normal.

Remdesivir is an adenosine nucleotide prodrug. It inhibits SARS-CoV-2 RNA polymerase. Eligibility criteria. Requiring supplemental oxygen, adults, adolescents ≥ 12 years of age and ≥ 40 kg, eGFR ≥ 30ml/min, ALT below 5 times the upper limit of normal at baseline. Discontinue in patients who develop ALT ≥ 5, ALT elevation accompanied by signs or symptoms of liver inflammation.

Please volunteer to support the research teams
RECOVERY study: Please contact Dr Teresa Costiello Contact or Dr Sundar Raj Ashok for advice.
REMAP CAP: Please contact Dr Taha Othmane, Dr Nabil Nizar, Dr Ajikumar Kavidasan or Dr Sundar Raj Ashok for advice.