Clinical guide for the management of critical care for adults with COVID-19 during the Coronavirus pandemic
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1 Introduction

This clinical guidance provides contemporary information on the care of critically ill adult patients with COVID-19 to practising clinicians at the bedside. Version 3 updates the previous NHS England guideline published on 8 April 2020.

NHS England have now passed responsibility for clinical guidelines related to COVID-19 to relevant professional bodies, which for this guideline are the Faculty of Intensive Care Medicine (FICM) and Intensive Care Society (ICS).

This document will be updated at regular intervals during the COVID-19 pandemic. Please always refer to the most up-to-date version, which will be available on the four organisations (Association of Anaesthetists, FICM, ICS, Royal College of Anaesthetists) hub.

This revised version contains important additions relating to:

- Use of anaesthetic machines for ventilation of critically ill patients
- Tracheostomy
- Extubation
- Secondary and co-infection
- Blood and thromboprophylaxis
- Acute Kidney Injury
- Neurological manifestations and management
- ICU acquired weakness.

The COVID-19 pandemic, caused by the SARS-CoV-2 virus, has placed an extraordinary burden on critical care, which is being met through the creation of surge capacity within and beyond hospital walls. Many non-specialist healthcare providers have supported critical care specialists to provide care. Staff safety and wellbeing is crucial in maintaining the resilience of critical care provision as the initial surge has passed and the requirement for a sustained response to the pandemic becomes clear.

This guide summarises the clinical characteristics of COVID-19 and offers advice on:

- Dealing with ‘surge’ including mutual aid
- COVID-19 clinical characteristics and specific treatments
- Clinical decision-making
- Management of respiratory failure
- Management of non-respiratory organ failure.

The effectiveness of most interventions in the context of COVID-19 is currently uncertain. This guide is informed by emerging information about COVID-19 management as well as best available evidence from non-COVID-19 patients. High quality multi-centre clinical trials are currently underway in patients with COVID-19 and will inform future versions of this guidance.
COVID-19 related clinical trials are important to rapidly develop an evidence base for this new disease and should be supported. The list of prioritised trials for COVID-19, including several in which critical care patients could be recruited (such as REMAP-CAP, GenoMICC and ‘RECOVERY-respiratory support’) can be found here.

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2 Dealing with surge

Supporting critical care surge capacity is requires different ways of working extending to:

- **Location**
  - Care of the critically ill being delivered in adapted areas within the hospital or purpose-built structures such as the NHS Nightingale facilities
  - Increased requirement for inter-hospital transfers within regions (‘mutual aid’ within critical care networks).

- **People**
  - Non-specialists delivering critical care, at times in adapted locations
  - Individuals and teams working in personal protective equipment (PPE).

- **Equipment**
  - Working with unfamiliar, rapidly procured and designed equipment (such as ventilators) and the associated training burden.

- **Consumables**
  - managing a greatly increased demand for materials such as drugs, haemofilters, PPE and oxygen
  - careful use and prudent allocation of resources, and learning from others’ experiences will be important (see Section 5: Management of respiratory failure).
- See also: Clinical guide for the management of surge during the coronavirus pandemic: rapid learning.

● Decisions
  - working within the clinical and ethical constraints imposed by high demand and finite resources (see Section 4: Clinical decision-making).

Surge capacity can be met through:

● Expansion within the hospital into temporary critical care resources (eg theatres, recovery areas, wards)
● Transfer of equipment (eg ventilators) between hospitals, particularly between the independent sector and NHS under the leadership and management of regional networks
● Re-purposing existing equipment (eg anaesthetic machines as ICU ventilators)
● Transfer of patients to another hospital within your critical care network (mutual aid)
● Regional ‘NHS Nightingale’ facilities
● Transfer of patients and resources between networks and regions

**Mutual Aid** has been implicit within the critical care networks for many years. The COVID-19 pandemic has highlighted the importance of collaboration and material support between intensive care units. Clinicians should not hesitate to seek advice and support (eg patient transfers, loan of equipment drugs and disposables) from colleagues in adjacent units when they feel that their own clinical experience and/or their local resources are stretched.

Safety and welfare of staff are essential if critical care provision is to remain resilient in the face of the demands of a sustained pandemic and should include:

● PPE guidance: PHE guidance
● Sustainable staffing patterns and rotas
● Attention to staff physical wellbeing, rest, diet and physical activity
● Attention to staff psychological wellbeing, particularly in relation to concerns about personal safety and responsibility (difficult clinical decision-making)
● Attention to the stresses on individuals working outside their usual scope of practice (eg non-specialist clinicians looking after critical care patients).
SARS-CoV-2 infection causing COVID-19 may manifest as:

- **Asymptomatic carriage (uncertain level)**
- **Acute mild/moderate illness (80%)** with:
  - Fever (≥37.8°C)
  - Cough
  - Shortness of breath
  - Sputum production
  - Non-specific: eg myalgia, malaise, anorexia, headache
  - Loss of smell and/or taste
- **Acute severe (15%) /critical illness (5%)**:  
  - Two lung phenotypes have been described, probably occurring sequentially:
    - Atypical viral pneumonitis = hypoxaemia with relatively compliant lungs
    - Classic acute respiratory distress syndrome (ARDS) = stiff lungs
  - Non-respiratory organ dysfunction:
    - cardiovascular failure (>25%)
    - acute kidney injury (25% needing RRT)
    - cardiac dysrhythmia (eg sinus tachycardia, AF, bradycardia)
    - neurological complications
    - liver dysfunction
  - Hyper-inflammation syndromes may occur – management uncertain, seek advice from local Severe Acute Respiratory Failure (SARF)/Extra-Corporeal Membrane Oxygenation (ECMO) networks.
  - Arterial, venous and pulmonary thromboembolism
- **Less common presentations:**
  - Diarrhoea and GI symptoms
  - COVID encephalopathy.
- **Risk factors for symptomatic disease and progression to critical illness:**
  - Age: over 50, substantial risk over 70
  - Male
  - Obesity
  - Ethnicity: black, Asian and minority ethnic
  - Comorbidities: cardiovascular disease, diabetes, chronic respiratory disease, hypertension, cancer, chronic kidney disease, immunosuppression.
Diagnosis

● History
  - Classical clinical picture (see acute mild/moderate illness above)

● Examination
  - Avoid use of stethoscope due to risk of viral contamination
  - Respiratory rate
  - Work of breathing
  - Cyanosis
  - Pulse oximetry.

● SARS-CoV-2 RNA Reverse Transcriptase - Polymerase Chain Reaction (RT-PCR)
  - From lower respiratory tract samples if possible
  - Beware false negative upper airway sample if clinical picture is typical.

● Diagnostic imaging
  - Chest X-Ray (CXR): bilateral patchy shadowing = interstitial pneumonitis
  - Computerised Tomogram (CT) chest:
    › May help establish the diagnosis if there is uncertainty
    › May provide useful supporting information on pulmonary pathology (eg pulmonary embolus) if done for another reason.

● Laboratory findings
  - Diagnostic utility:
    › Low lymphocyte count
    › Normal Procalcitonin
    › Creatinine Kinase - elevation = myositis/myocardial involvement
    › Troponin - elevation = myocardial involvement.
  - Severity of illness markers (not all necessary):
    › Elevated D-dimers
    › High neutrophil-lymphocyte ratio
    › Low albumin
    › Elevated Troponin/Brain Natriuretic Peptide (BNP)
    › Elevated Ferritin.
  - Check Lactate Dehydrogenase and Ferritin if hyperinflammation syndrome suspected
  - C-Reactive Protein (CRP)
    › Uncertain value
    › Rising CRP may indicate bacterial infection or disease progression.
Management
Supportive care is the mainstay of COVID-19 management.

Anti-viral therapy
- Remdesivir may be considered for patient admitted to critical care
- For dosing, Remdesivir should be given as a 200mg loading dose IV then 100mg IV once daily for the next 9 days if ventilated or 5 days of not ventilated.
- Remdesivir is currently available under the early access to medicines scheme (EAMS) and approved indications will be updated regularly.

Steroid therapy
- The RECOVERY trial has provided initial results on dexamethasone in COVID-19.
- Dexamethasone 6 mg once per day (either by mouth or by intravenous injection) for ten days reduced deaths by one-third in ventilated patients and by one fifth in other patients receiving oxygen only.
- There was no benefit among those patients who did not require respiratory support.
- Although a full paper has not yet been published, the CMOs of England, Wales, Scotland and Northern Ireland have stated that ‘...given this clear mortality advantage, with good significance, and with a well known medicine which is safe under these circumstances we consider it is reasonable for practice to change in advance of the final paper.’
- Where patients require corticosteroids for other indications (either at replacement doses for known adrenal insufficiency or as a treatment for another underlying condition such as asthma or Chronic Obstructive Pulmonary Disease (COPD)), they should not be withheld.

Research for other specific therapies and vaccines are underway.

Other Anti-SARS-CoV-2/COVID-19 therapies should only be administered within the context of a nationally approved trial. COVID-19 related clinical trials should be supported to rapidly develop an evidence base for this new disease.

Routine antibiotics
- Routine antibiotics are not recommended for uncomplicated COVID-19.

Treatment of other conditions in the context of COVID-19
- Careful attention to antimicrobial stewardship: antibiotics should be considered if there is suspected bacterial super-infection.
- Take care not to neglect treatment of exacerbation of any underlying conditions (eg heart failure, COPD, diabetes).
- Consider other possibilities in the differential diagnosis for patients with possible COVID-19.
Impact of non-steroidal anti-inflammatory drugs (NSAIDs), ACE-inhibitors and ARBs on COVID-19

- There is uncertainty about the impact of ACE-inhibitors and Angiotensin Receptor Blockers (ARBs) on the severity of COVID-19.
- There is currently no evidence that the acute use of NSAIDs causes an increased risk of developing COVID-19 or of developing more severe COVID-19.
- Acute use of NSAIDs in people with or at risk of COVID-19 should include a balanced assessment of the potential risks and benefits using each medicine’s product information. If used, the lowest effective dose of NSAID should be used for the shortest period required to control symptoms.
- Where patients are already taking these medications for other conditions, continuing treatment is recommended by national and international bodies, including the Renal Association UK, the European Renal Association, the European Society of Cardiology and the European Medicines Agency.

4 Clinical decision-making

General comments

- Intensive care decision-making should be consistent with normal ethical and legal frameworks within the NHS.
- All patients, irrespective of their presenting diagnosis, should be treated respectfully and equally and should receive the best available care. Patients should not be treated differently because of anticipated future pressures: it is important to focus on current clinical demands and available resources.
- Doctors should consider policy guidance from the GMC about clinical decision making during the current pandemic.
- Assess what care is likely to provide benefit to the patient, taking into account the best available evidence on factors that predict this and applying it to the specific situation of the patient being treated.
- Decision support tools developed in the context of COVID-19 are available (NICE pathway) and may help guide these discussions and decisions. As more evidence and experience of managing COVID-19 becomes available, these tools will become more valid and relevant for patients within the NHS.

Referral and admission to intensive care or palliative care

- Treatment escalation plans (TEP) should be discussed with patients, and/or their relatives, at the first opportunity and be clearly documented. TEPs should take account of the person’s values and of the goals of treatment.
- Referral for consideration of admission to ICU should be considered carefully by a senior clinician, using current guidance (eg NICE pathway, local and national guidelines) as an aid.
- The decision to admit to intensive care should be made by an intensivist. When an intensivist is not available, a senior physician with expert knowledge of intensive care interventions and
outcomes should decide. This decision should be discussed with the patient (or next of kin, personal representative, or legal power or Independent Mental Capacity Advocate (IMCA) as determined in each devolved nation’s legal framework) and the decision and discussion clearly documented by the referring or ICU team as appropriate.

Treatment decisions

- Good practice in critical care routinely involves continuous assessment of every individual patient’s progress, the likelihood of an outcome that is acceptable to the patient, and the adjustment of treatment plans in the light of these factors.
- On admission to intensive care the patient’s expectations and the goals of treatment should be reviewed.
- **All patients must have daily review by a physician and discussion with an expert in intensive care to assess whether the goals of treatment are being met and whether the outcomes expected at admission remain realistic.**
- Regular communication updates with the patient’s representative by informed members of the critical care team are recommended. Consideration should be given to the use of approved video-conferencing.
- Where treatment is limited or withdrawn, there must be clear and complete documentation of the rationale for any decisions and documentation of discussions with the patient or their representative (as determined by each nation’s legal framework) and any other clinical staff involved.
- Where treatment is limited or withdrawn, the priority of care will become best possible end-of-life care for the patient. The benefit of involving a palliative care team should be considered, especially if the patient is managed outside the intensive care unit.

5 Management of respiratory failure

Oxygen therapy

- Avoid hyperoxaemia in patients receiving supplemental oxygen.
- Generally, aim for SpO$_2$ 92-96%, although the target will be lower in some patient groups, eg those with chronic obstructive pulmonary disease (COPD).
- An SpO$_2$ target of 90-93% is acceptable in patients with visible continuous pulse oximetry in an appropriately monitored care environment with trained staff to monitor for clinical deterioration.
- **High flow oxygen delivery devices may place a strain on oxygen supplies with the risk that site supply failure may occur.** This can be difficult to predict, even if the pressure and total flow are known.
- Eliminate waste by ensuring oxygen flowmeters and high-flow devices are switched off when not attached to patients.
High flow nasal oxygen

- High flow nasal oxygen or similar high flow devices are of uncertain utility:
  - Local maximum oxygen outlet delivery limitations preclude widespread use (see above)
  - Risk of environmental viral contamination is unknown but may be higher than that associated with invasive mechanical ventilation
  - Monitoring should be with continuous pulse oximetry in a care environment with trained staff to monitor for clinical deterioration.

CPAP and NIV

- Please see the specialty guide for [more details here](#).
- Use only MHRA approved devices
- Caution must be exercised with high flow CPAP devices due to concerns about oxygen utilisation (see above).
- PPE should be consistent with PHE guidance for an aerosol generating procedure.
- See PHE IPC guidance here
- CPAP devices (via a non-venting face mask or helmet) may be trialled to assess whether invasive mechanical ventilation can be avoided in selected patients under the following circumstances:
  - Monitoring should be with continuous pulse oximetry in a care environment with trained staff to monitor for clinical deterioration.
  - Failure to respond to a CPAP trial (deterioration in gas exchange; high work of breathing) is an indication for early intubation and invasive mechanical ventilation in patients considered appropriate for escalation.
  - Low-flow CPAP devices using entrained oxygen may be suitable for patients with a lower oxygen requirement (FiO2 < 0.4).
  - Some milder severity patients may improve symptomatically after short periods (1-4 hours) of CPAP with corresponding reductions in FiO2, respiratory rate and work of breathing to maintain adequate SpO2 values.
- Patients who present as too critically unwell, or who do not respond clinically to a CPAP trial (deterioration in gas exchange, high work of breathing), and/or do not tolerate CPAP, should receive early intubation and invasive mechanical ventilation according to appropriateness of escalation.
- Patients may look comfortable on CPAP in the early phase of illness when lung compliance is normal. Elevated or increasing spontaneous minute ventilation may be an indicator of clinical deterioration or disease progression.
- For some patients, CPAP or NIV will form the appropriate ceiling of treatment. Identify these patients early to prevent inappropriate escalation to invasive support.
- NIV (BiPAP) is not generally indicated in hypoxaemic respiratory failure but may be considered in certain patient groups with Type 2 respiratory failure (eg COPD).
An appropriate antimicrobial filter should be located on the expiratory limb of any NIV or CPAP device.

Due to a risk of environmental viral contamination, where possible deliver mask ventilation in an isolated environment (negative or neutral pressure room, check the air exchanges in positive pressure rooms, or cohort in restricted access areas).

Awake prone positioning may improve V/Q mismatch, oxygenation and work of breathing and may be combined with CPAP or NIV.

The type and location of respiratory support following extubation (e.g., CPAP, high or lower flow O₂) should be informed by clinical assessment, repeat testing of SARS-CoV-2 status (where available), and balancing the risks of cross-infection with the benefits of different approaches.

Consideration should be given to cohorting extubated patients according to SARS-CoV-2 status both within ICUs and in step-down units.

Intubation

Follow intubation guidance from: https://icmanaesthesiacovid-19.org

Intubation should be performed by a skilled operator wearing appropriate PPE for an aerosol-generating procedure. See PHE IPC guidance here

Mobile Emergency Rapid Intubating Teams (MERIT) with appropriate portable equipment, PPE and protocols are recommended.

Clamping of endotracheal tubes (e.g., during exchange of breathing systems) may be useful to minimise the risk of viral contamination of the environment but can result in damage to the tube or pilot tube or damage to the plastic of the 15mm circuit connector if clamped too close to the end of the ETT. There may be a risk of the ETT subsequently kinking at the point where the tube has been repeatedly clamped.

For ET tubes with sub-glottic suction ports, clamping tubes at 90 degrees to the plane of the sub-glottic channel may reduce the risk of sub-glottic channel fracture

Any adverse incidents should be reported through local and national reporting systems to spread learning from events across the healthcare system and to help prevent future incidents.

Mechanical ventilation

Ensure use of an antimicrobial filter within the circuit or placed on the expiratory limb or ventilator exhaust. **Note that filters represent an airflow obstruction risk when saturated and regular assessment and replacement is advised.**

Heated humidifiers can cause rapid saturation of in-line filters and the combination should be used with caution. If possible, when using a heated humidifier circuit, attach the antimicrobial filter to the ventilator exhaust.

Use of dry circuits with HME filters can cause secretion build-up and obstruction of tracheal tubes. Regular nebulized saline (normal- or hypertonic) ± mucolytics (in-line with respiratory circuit) may be useful but may contribute to circuit obstruction through saturation of filters and salt crystal build-up within ventilator expiratory blocks.

**Airflow obstruction due to saturation of antimicrobial filters, particularly when use with heated humidifiers or nebulisation may be indicated by sudden or progressive deterioration in:**
i minute ventilation

ii capnography

iii airway pressures

- Use in-line suction systems where possible.
- Avoid inadvertent ventilator circuit disconnections by ensuring all connections are ‘tight’.
- Manual ventilation (eg ‘hand-bagging’ with a bag-valve-mask or anaesthetic circuit plus face mask) should be avoided where possible due to concerns about aerosol generation and infection risk.
- Clamp the tracheal tube and set ventilator to pause/standby during any planned circuit disconnection, eg switching between ventilators, during proning/deproning manoeuvres, replacing the antimicrobial filter, or inserting a bronchoscope into the catheter mount.

Issues specific to ventilation with anaesthetic machines:

- Fully specified intensive care ventilators should be used in preference to anaesthetic machines when these are available.
- Mutual aid should be used to source intensive care ventilators from other centres if required, in preference to using locally available anaesthetic machines, where possible.
- Anaesthetic machines should ideally be reserved for patients with the lowest critical care acuity scores and whose lung compliance makes them easier to ventilate.
- It may be necessary to move patients from an anaesthetic machine ventilator to a conventional critical care ventilator if the patient’s lung compliance deteriorates.
- Anaesthetic machines are designed to be restarted and self-tested every 24 hours to ensure proper calibration, accuracy and performance. An interval of up to 72 hours is permitted during the pandemic according to guidance from most manufactures.
- Anaesthetic machines needs to be configured for long-term use with attention to gas supplies and removal of nitrous oxide.
- Antiviral filters must be used to protect staff and to prevent contamination of the machine.
- Oxygen concentrations in the circuit must be monitored as well as $\text{FiO}_2$, $\text{FiCO}_2$ and $\text{EtCO}_2$ in all patients.
- The default alarm limits are not suitable for caring for critically ill patients and will need adjustment.
- Fresh gas flows should replace patient oxygen consumption and losses due to leaks and gas sampling i.e. at least $\text{Minute Volume} \times \text{FiO}_2 + 1 \text{ litre per minute}$ to avoid rebreathing and generation of excess humidity.
- An increase in the fresh gas flow every four hours is recommended to keep the internal components of the machine dry.
- Regular inspection of the circuit for accumulation of water or collapse of the reservoir bag/bellows is essential.

Please see specific guidance on use of anaesthetic machines [here](#).
Management of early (pneumonitis) phase

- Compliance is normal, and recruitment manoeuvres often do not improve gas exchange.
- PEEP < 10 cmH₂O is often sufficient. A high PEEP strategy may be harmful.
- Aim for lung protective ventilation (6 mL/kg), including driving pressure < 15 cmH₂O (driving pressure = plateau pressure – PEEP).
- **Neuromuscular blockade** to avoid high transpulmonary pressures and further lung injury is advised if there is ventilator dysynchrony or a high spontaneous minute ventilation.
- Consider inhaled pulmonary vasodilators (e.g., nitric oxide, nebulised iloprost or epoprostenol) to improve V/Q mismatching.
- Improvements in oxygenation can often be achieved with prone positioning (see below).

Management of later (typical ARDS) phase

- Compliance is low and recruitment may be useful.
- Follow established **ARDS management guidelines** including:
  - lung protective ventilation
  - conservative fluid management strategy (**beware hypovolaemia**)
  - prone positioning (see below).
- Consider neuromuscular blockade by bolus or infusion.
- Consider careful lung recruiting manoeuvres, such as PEEP escalation and recruiting ventilator modes.
- If other strategies fail, consider referral for ECMO (see below).

Prone positioning

- A beneficial response to prone positioning is often seen in awake patients (either on an oxygen face mask alone or receiving CPAP/NIV), or ventilated patients in either pneumonitis or typical ARDS phases.
- Proning should take place in an appropriately monitored care environment with trained staff. Turn head regularly (e.g., 3 hourly) and be careful about potential injury to eyes, pressure areas, shoulders and obstruction/displacement of endotracheal tube/tracheostomy.
- Proning is recommended for 16-18 hours per day (longer may be acceptable) – multiple episodes over the course of up to a week may be beneficial.
- Development of a 'Proneing Team' is advised to improve efficiency when substantial numbers of patients are requiring turning prone/supine and head turning. The Proning Team may comprise staff from non-ICU backgrounds under supervision of a suitably skilled ICU member of staff.

Tracheostomy

- Advice for care of patients currently with a tracheostomy is available.
- Airway oedema is common (see comments below under extubation).
- Decision making in relation to new tracheostomies needs to balance the risk of infection (aerosol spread of SARS-CoV-2) with the best management for the patient within the available resources.
● Tracheostomy may:
   - facilitate weaning from mechanical ventilation and patient comfort
   - allow reduced use of sedation and, consequently, pressor medication
   - enable safe management with lower staffing and equipment levels.

● Staff must be able to care for tracheostomised patients.

● Tracheostomised patients who remain SARS-CoV-2 +ve carry an on-going risk of viral aerosolization.

NIV and weaning

● There may be a role for NIV or CPAP (including for patients with tracheostomies) to aid weaning from ventilator support (and the requirement for sedation).

● NIV machines may be used in place of ICU ventilators where there are equipment shortages.

Extubation

● Need for reintubation is associated with airway swelling, tenacious secretions, weakness and delirium.

● Early extubation (< 7 days) is more likely to be associated with failure.

● To minimise reintubation rates, careful and comprehensive clinical assessment should be undertaken prior to any planned extubation.

● Extubation should be delayed until there is a consistently improving trajectory in the following:
   - breathing pattern, including markers of respiratory and cough strength
   - ability to self-clear secretions
   - chest radiology
   - markers of inflammation and thrombosis
   - oxygenation and mean airway pressure & PEEP.

● Spontaneous breathing trial, RSBI, NIF and P0.1 may be useful in monitoring for injurious spontaneous breathing patterns and readiness to extubate.

● ‘Cuff leak’ tests may be useful for assessing airway swelling, but be aware that there may be an associated aerosol generation risk.

● Consider upper airway visualisation prior to extubation to assess for swelling.

● Dexamethasone (or methylprednisolone) may be used to reduce airway oedema when present.

● In appropriate patients, tracheostomy should be considered in those who have been reintubated or failing to meet the extubation criteria after more than 14 days of ventilation.

Extracorporeal membrane oxygenation (ECMO)

● Follow published pandemic guidance and thresholds for referral to the ECMO network here.

● ECMO referral data will be communicated via a single platform here.

● ECMO network regional centres can be contacted for advice and guidance.
Aerosol-generating procedures (AGPs)

- AGPs such as intubation and extubation, facemask ventilation, circuit disconnection, bronchoscopy, tracheostomy formation and some physiotherapy procedures will increase the risk of environmental viral contamination. Please see the PHE website for the full list and guidance on appropriate PPE.

- Nebulisers are not considered an AGP but, within critical care, use should be confined to within a closed ventilator circuit.

Corticosteroids

- Patients with a persistent lung injury evidenced by radiographic changes, ventilator mechanics and persisting or rapidly worsening COVID-19 inflammatory markers may respond clinically to corticosteroids. It is uncertain at present whether this impacts positively or negatively on outcomes, or what dosing regimen (eg short-course pulsed methylprednisolone or a more prolonged ARDS-type regimen) is superior.

Secondary or co-infection

- Secondary or co-infection with bacterial or fungal infection may be seen.

- Standard markers of Ventilator Acquired Pneumonia (VAP) are less helpful in COVID-19 as fever and rising CRP are often seen as part of the SARS-CoV-2 inflammatory process. The latter is suggested by concurrent rises in ferritin, LDH, BNP and troponin.

- Perform regular microbiological surveillance, including fungal biomarkers (β-D-glucan and galactomannan), if available.

- PCT may be useful in helping to guide decision-making around antimicrobials.

6 Management of non-respiratory organ failure

Cardiovascular

- ‘Palpitations’ and ‘chest tightness’ can be presenting features of COVID19.

- Both antecedent cardiovascular disease (CVD) (for example, hypertension, cardiomyopathy or coronary vascular disease; found in >30%) and raised cardiac troponin (TnT) (found in> 25%) are associated with mortality.

- Mortality is doubled in the presence of CVD, is further elevated if TnT is raised in the absence of CVD, and is elevated 10-fold if CVD is present and TnT elevated.

- Raised NT-proBNP levels may occur and are associated with poorer outcome.

- Raised TnT may occur via diverse mechanisms (ACE2, hypoxia/oxidative stress, cytokines, or microvascular damage).

- Myocarditis is diagnosed in some cases, although histological evidence is currently weak. A raised TnT alone is not sufficient for this diagnosis, and this remains a diagnosis of exclusion.

- Tamponade can rarely occur. ECG and echocardiography may help with diagnosis.

- Cardiac contractile failure (‘heart failure’) can occur, most commonly later in the disease course.
● Remember: acute coronary syndromes can still occur. Diagnosis can be difficult given that raised TnT is common. Echocardiography (regional wall motion abnormality) and ECG may help: seek expert cardiological advice.

● In cases of cardiac arrest, chest compressions may be commenced. Whilst PHE do not consider chest compressions to be an AGP, the current position of the Resuscitation Council UK is that chest compressions are an AGP and that PPE should be worn.

● Definitive airway management will generate aerosols and should not be performed until all staff are wearing appropriate PPE. The availability of ‘grab bags’ and rehearsed resuscitation teams can help with the speed of response. Airway interventions must be carried out by very experienced staff. Outcomes from cardiac arrest appear poor (<5% survival).

● In cases of significant hypotension or circulatory shock, standard circulatory assessment (fluid responsiveness, cardiac output assessment) and administration of appropriate fluid bolus(es) and/or pressor (where appropriate) should occur.

● Balanced crystalloid electrolyte solutions are preferred to saline 0.9% or colloids for both fluid challenges and continuous infusion.

● While fluid overload should be prevented and more conservative administration may help improve respiratory function, this should be carefully balanced against the risk of inducing acute kidney injury.

● Norepinephrine (or metaraminol or vasopressin where norepinephrine is unavailable) appears to be a reasonable first-line pressor, pending circulatory assessment (above).

Renal

● AKI requiring RRT is reported in >25% of COVID-19 patients admitted to critical care.

● Direct SARS-CoV-2 infection of the proximal tubule and other renal cells is now recognized. Intra-renal microthrombi and glomerular pathologies have also been described.

● SARS-CoV-2 RNA has been detected in urine.

● Haematoproteinuria is a frequent feature.

● Care should be exercised in ‘running patients too dry’ in an effort to spare the lungs.

● Renal perfusion may be compromised by high airway pressures and high PEEP.

● Myoglobinuria occurs in some patients with COVID-19 and may be a risk facture for AKI.

● There is no specific therapy for COVID-19 associated AKI.

● Standard renal replacement therapies are appropriate but may need to be modified during surge periods.

● In patients who are prothrombotic (as evidenced by filters clotting for example), full systemic anticoagulation is generally necessary even when citrate anticoagulation is used.

● Medical management of acute kidney injury, including diuretics for fluid overload and bicarbonate to correct metabolic acidosis, may be useful to delay the requirement for renal replacement therapy.

● If RRT machines are in high demand, consider mutual aid. If haemofiltration sets are in high demand, use for 24–48 hours. Guidance on RRT can be found here.

● In patients recovering from AKI, serum creatinine results should be interpreted with caution due to the high prevalence of muscle wasting.
Thromboprophylaxis
- Prothrombotic phenotype is common (high fibrinogen and D-dimer).
- Pay great attention to thromboprophylaxis including non-pharmacological methods (intermittent pneumatic compression stockings, TEDS).
- **Have a high index of suspicion for the presence of deep venous or pulmonary vascular thrombosis and investigate urgently where clinical suspicion is raised.**
- At least 30% of ICU patients may develop a thromboembolic event (VTE in 25% of all patients, arterial thrombotic events in 3.7% (95%CI 0-8.2%). Pulmonary emboli and thromboses are common.
- Consider pulmonary embolus if sudden deterioration in gas exchange.
- Further guidance can be found here.

Gut
- Stool SARS-CoV-2 RNA is found even after respiratory tract clearance and is a potential source of infection.
- 80% of patients suffer loss of appetite, and a further 40% other GI symptoms: diarrhoea (2-35%), nausea (17%) or vomiting (1-10%).

Feeding
- **Protein/Energy:** Use local targets. Adjust for Propofol (1.1kCal/ml) & citrate anticoagulation during RRT (2 L/h; 550 kcal/24h for Prismaflex; 300kcal/24h for Multifiltrate).
- **GI Intolerance:** Beware QT prolongation (eg metoclopramide/erythromycin with hydroxychloroquine/amiodarone). Where needed, parenteral nutrition may be easier than post-pyloric tube placement.
- **Limited pump availability:** Consider a) concentrated feed + higher rate +12-hour pump sharing (sanitize between patients) b) concurrent water + feed together where needed) syringe bolus feeding 6x/day d) Gravity feeding.

Gastroprotection
- Despite lower platelet counts, patients appear prothrombotic.
- Use local gastroprotection practice.
- Consider once daily dosing until 48 hours after feed established where feasible.

Liver
- About half may get raised ALT/AST/GGT/bilirubin levels – no specific intervention is advocated.

Neuromuscular
- Up to one third of patients may have neurological manifestations.
- Seizures may occur.
- Stroke (perhaps 1%) and reduced consciousness (<15%) tend to occur late in disease.
- Reports of encephalitis are beginning to appear.
Axonal neuropathy is reported at circa 2 weeks of illness.
Muscle wasting is common.
Practical guidance on the use of nerve conduction testing/EMG is now available.
Vasculitis may affect skeletal muscle.
Muscle pain and fatigue occur in over 35% of patients with COVID-19 disease.
Skeletal CK may be elevated. Routine measurement is recommended, with origin confirmed (compare with cardiac troponin levels/do CK isoforms where indicated and readily available).
ICU Acquired Weakness (due to neuromuscular impacts) appears prevalent (25-50%), impacting on weaning and rehabilitation. Once off sedation, perform daily Chelsea Critical Care Physical Assessment (CPAX) Score. Medical Research Council Sum Score (MRC-SS: p3) to diagnose ICU-AW diagnosis, will aid stratification for rehabilitation. Mobilise according to local practice.
A high incidence of delirium is expected.
- Use non-pharmacological interventions: ear plugs at night, eye pads to limit light exposure at night, orientation, sleep hygiene (including normalisation of day/night cycle), objective pain assessments and mobilisation
- Use of pharmacological agents may increase mortality, especially where long Q-T interval can occur (eg beware use with hydroxychlorquine and/or amiodarone and prokinetics).

7 Further guidance

Nutrition guidelines
- British Association for Parenteral And Enteral Nutrition (BAPEN)
  Route of Nutrition Support in Patients Requiring NIV & CPAP During the COVID-19 Response
- British Dietetic Association (BDA)
  Critical Care Specialist Group COVID-19 Best Practice Guidance: Enteral Feeding in Prone Position

After-care needs
- NHS England
  After-care needs of inpatients recovering from COVID-19