AWAKE PRONE

Frequently Asked Questions

Set Up

Is there a minimum recruitment target?

Our recruitment target is based on 60 sites recruiting 1.25 patients a month.

Are there multiple accruals if a patient participates in more than one CoReCCT domain (trial)?

Yes. There is one accrual per CoReCCT trial. Each trial has its own CPMS ID. Recruitment uploads, however, will be managed by Warwick CTU. Sites only need to mark themselves as 'open to recruitment' on their local portfolio management system.

What database will the study be using?

A bespoke Warwick CTU built database. This will consist of Core and domain specific parts. The Core Database will house data and CRFs shared across CoReCCT domains; the domain specific database will house data and CRFs specific to each domain. Database access will be controlled by the domain specific delegation logs you appear on.

Screening & Eligibility

Who confirms eligibility?

Eligibility can be confirmed by anyone that is suitably trained and experienced and who has been delegated responsibility to undertake this role by the PI.

Which patients should be entered on the screening log?

Please record details of patients that meet all the inclusion criteria, and who meet one or more of the exclusion criteria (making them ineligible). On the log, select which of the exclusion criteria they met.

Patients that are randomised do not need to be included on the screening log because they have not met any of the exclusion criteria and are therefore eligible.

Patients that do not meet all of the inclusion criteria do not need to be recorded on the log.

What is the target population for Awake Prone?

Awake Prone wants to recruit a broad spectrum of patients with acute hypoxaemic respiratory failure.

Whilst we expect most patients will have a community acquired or hospital acquired pneumonia, we also expect to recruit patients with other causes of respiratory failure, such as post-surgical respiratory failure and indirect causes of respiratory failure (e.g. extra-pulmonary sepsis/pancreatitis).

How does the study define acute hypoxaemic respiratory failure?

In Awake Prone, we define acute hypoxaemic respiratory failure as having a $SpO_2 \leq 94\%$ whilst receiving ≥40% supplemental oxygen for a sustained period of time.

The reason for this requirement is to exclude patients who require a higher amount of oxygen for a short period of time, such as following mobilisation. The presence of acute hypoxaemic respiratory failure for at least one hour would meet this definition, but it is reasonable to use clinical judgement when making this assessment.

Eligibility should be re-checked just prior to randomisation to ensure the patient continues to have acute hypoxaemic respiratory failure.

Is an arterial blood gas required to determine eligibility?

No.

If an arterial blood gas is taken as part of routine care prior to randomisation, we will ask you to record details on the case report form.

What if there is a discrepancy between SpO_2 and SaO_2?

Pulse oximeters may over-estimate SpO_2, compared with SaO_2 as measured by a blood gas analyser, particularly in individuals with darker skin pigmentation.

Where a patient has an arterial blood gas measured as part of routine care, it is acceptable to use either the SpO_2 or SaO_2 for the purposes of determining eligibility.

How should eligibility be determined in patients receiving ≥60% O_2 with SpO_2>94%?

You should attempt to wean the oxygen percentage, in line with standard care, to determine whether the patient meets the eligibility criteria.

If it is considered unsafe to attempt to wean the oxygen percentage and it is clear that the patient would fulfil the eligibility criteria if the oxygen percentage was weaned, then the patient can be deemed eligible on this basis.

Will there be a table to reference for conversion from litres of oxygen to 40% similar to other studies such as RECOVERY?

No, we will not be creating a table to convert lpm to % O_2. We are keen to be pragmatic and are aware that many sites may have developed their own conversions, as such we do not want to cause confusion. We assume most patients will receive O_2 via a device that delivers a specific O_2% (eg. humidified system / venturi).

Are patients with hypercapnia eligible?

Yes.

If a patient meets the criteria for acute hypoxaemic respiratory failure and is hypercapnic, then they are potentially eligible for the study.

How do we determine eligibility if the patient's target SpO_2 is lower than 94%?

Some patients, due to conditions such as chronic lung disease, may have a lower SpO_2 target. These patients are potentially eligible provided that they are on at least 40% oxygen.

Does a potential participant need to be reviewed by a critical care clinician to determine suitability for tracheal intubation?

No.

The eligibility criteria requires that the patient would be eligible for tracheal intubation in the event of physiological deterioration. Given the study's target population is at high risk of deterioration, we would recommend that the clinical team consider treatment escalation planning as part of standard clinical care.

For Awake Prone, this process is not mandated and does not require referral to critical care. If the patient's own clinical team has not recommended against tracheal intubation, then the patient is potentially eligible.

Are patients with a DNACPR potentially eligible?

Yes. Where a patient has a DNACPR but would be eligible for tracheal intubation in the event of deterioration.

The patient has been invasively ventilated during the current admission; are they potentially eligible?

The patient will only be potentially eligible for Awake Prone if they were intubated only for the purpose of facilitating a procedure or operation (e.g. imaging/ surgery/ endoscopy).

Is a patient potentially eligible if they are receiving non-invasive respiratory support?

Yes.

Patients receiving CPAP/HFNO/NIV are potentially eligible provided they meet criteria for acute hypoxaemic respiratory failure.

We collect key settings for each type of non-invasive respiratory support at baseline (e.g. flow for HFNO).

Is the participant eligible if they have pulmonary odema?

If a potential participant has acute hypoxaemic respiratory failure caused by pulmonary odema that is wholly explained by heart failure, then the individual is not eligible for Awake Prone.

Individuals may be potentially eligible for Awake Prone if their acute hypoxaemic respiratory failure is caused by pulmonary odema not wholly attributable to heart failure (e.g. combination of heart failure and another cause), or if their respiratory failure is attributable to both pulmonary odema and another cause (e.g. infection).

This should be a clinical assessment based on the available clinical information. Additional testing (e.g. point-of-care ultrasound) is not required to make this assessment.

Can patients with COVID-19 participate? Is a COVID-19 test required to determine eligibility?

If the primary cause of the patient's acute hypoxaemic respiratory failure is COVID-19 pneumonitis, then the patient is not eligible as we would expect awake prone positioning to form part of their routine clinical care.

If an individual is found to have COVID-19 by PCR test, but this is not deemed to be the cause of their acute hypoxaemic respiratory failure then the individual is potentially eligible.

A COVID-19 test is not required to determine eligibility.

What happens if the participant acquires COVID-19 during the hospital stay?

If COVID-19 is not the primary cause of the respiratory failure, then the patient is still eligible for the Awake Prone trial – this will require clinical judgement. If a participant develops COVID-19 following randomisation, then you will need to make a clinical judgement as to whether COVID-19 has become the primary cause of respiratory failure, such that there is now an absolute indication for awake prone positioning.

How do we determine patient willingness to attempt awake prone positioning?

Patients should be asked if they would be willing to attempt awake prone positioning if they were randomised to the awake prone positioning arm of the study. If they express a willingness to try, then they are potentially eligible.

What are contraindications to awake prone positioning?

The key issue to consider is whether there are patient or contextual factors that may make awake prone positioning unsafe. Patient contraindications to awake prone positioning include open abdominal wounds, unstable spinal fractures, and haemodynamic instability. Certain types of thoracic surgery, ENT, or cardiac surgery may also be contraindications to awake prone positioning.

Are all causes of acute hypoxaemic respiratory failure potentially eligible?

Yes, subject to the notes on COVID-19 and pulmonary oedema detailed above.

Once a patient meets the study eligibility criteria, how quickly do they need to be consented and randomised?

The study protocol does not mandate that patients are recruited within a specific period of time. The intervention of awake prone positioning is likely to be most effective when implemented early, so we would encourage sites to recruit as early as possible.

Consent

Is consent taken multiple times for patients taking part in more than one CoReCCT trial?

Yes, consent is required for each CoReCCT trial.

Who can receive consent/ consultee agreement?

Consent/ consultee agreement can be received by anyone that is suitably trained and experienced and who has been delegated responsibility to undertake this role by the PI.

Will there be deferred consent?

No, although we will make use of consultee agreement for any participant unable to consent themselves. This can be a relative/friend or professional consultee. It is also necessary to ensure participant is willing to attempt awake prone position.

Care delivery following randomisation

In which clinical settings can the intervention be delivered?

The study is designed to be delivered in any clinical setting in which it can be safely delivered in your hospital. During the set-up stage, we will confirm with you the target areas for recruitment and intervention delivery.

Following randomisation, what SpO_2 target should we aim for?

The SpO_2 for each patient should be set by the clinical team.

The study does not mandate a specific SpO_2 target.

Are there any treatments that are not permitted during the study?

No.

The study randomisation only influences patient position. All other treatments may be determined by the clinical team. These include non-invasive respiratory support (and settings), oxygen delivery device, antibiotics, and steroids. We do ask you to record key details about some treatments on the case report form.

Does the study require that any arterial blood gases are collected?

No.

We will, however, ask you to record the results of routinely collected arterial blood gases at key time points.

Does the study stipulate when patients should be intubated?

No.

The decision to intubate is a complex clinical decision that will be influenced by factors such as patient physiology, patient trajectory, and patient wishes. The decision to intubate is entirely at the discretion of the clinical team in collaboration with the patient.

What happens if a participant is transferred to a different hospital that is running Awake Prone, do they continue proning there?

If the receiving hospital is part of your NHS organisation and it is possible to continue the randomised allocation at the new hospital, then please continue, wherever possible, with

the randomised allocation at the receiving hospital unless it has been discontinued for another reason (e.g. tracheal intubation).

Awake prone positioning

How quickly should awake prone positioning be started after randomisation?

As soon as possible.

What is the target duration of awake prone positioning per day?

The target duration is a minimum of 8 hours per day. This can be achieved through a single prolonged period or multiple shorter periods. Each period should be at least one hour.

How should the patient be positioned outside of time spent in the awake prone position?

Outside of times spent in the awake prone position, patients and their clinical teams can choose how they are positioned. This includes sitting out of bed, where appropriate.

What happens if the patient cannot tolerate awake prone positioning?

Patients should initially be positioned in the full prone position. If they find the position uncomfortable, we suggest the following steps:

1) Try and find out what the patient finds uncomfortable. This might be addressed through repositioning pillows, choosing a softer/ firmer pillow, or changing the tilt of the bed.

2) Reassure the patient that we know the position can be uncomfortable and try to encourage them to persevere if possible. If the patient's oxygen saturations have improved since lying in the prone position, it may be helpful and reassuring to tell them this.

3) Consider whether other interventions may be helpful to improve comfort, such as anti-emetics if feeling nauseous.

4) If these are unsuccessful, attempt the 3/4 prone position instead. Try and repeat the steps above to optimise comfort in the 3/4 prone position.

5) If the patient continues to find the prone position difficult to tolerate, then please try returning to a semi-recumbent position and trying again later.

What if the participant has spent no time proning today?

Record this on the proning log including a reason if possible.

Stopping the intervention

For someone randomised to awake prone positioning, what are the reasons for stopping the intervention?

The protocol lists seven reasons for stopping the intervention:

1) 120 hours from randomisation,

2) Tracheal intubation,

3) Participant recovery,

4) Participant decision to stop intervention,

5) Development of contraindication to awake prone positioning,

6) Participant transferred to care setting where intervention could not be delivered, or

7) Participant transferred to another hospital.

What is meant by participant recovery?

Participants may recover before the end of the intervention period. We have not stipulated a definition of recovery but expect that this will be defined by the clinical team in collaboration with the participant. Potential markers of recovery include:

- Normalisation of respiratory rate
- Decreased shortness of breath
- Improvement in SpO_2 and reduced oxygen requirement

In general, an $SpO_2 \geq 94\%$ or more on $\leq 35\%$ supplemental oxygen would be a reasonable marker of recovery. It is expected that any clinical improvement is sustained after moving to a semi-recumbent position.

If the patient deteriorates after having been determined to have recovered, then further use of the awake prone position will be at the discretion of the clinical team.

What is meant by development of a contraindication to awake prone positioning?

This means the development of any clinical condition which would make use of awake prone positioning unsafe.

For example, if a patient requires surgery and returns from theatre with a large abdominal wound, then this would likely be deemed to be a contraindication.

What happens if following randomisation the participant's treatment escalation plan is reviewed, and they are determined to not be appropriate for tracheal intubation?

Where possible, the awake prone positioning intervention should be continued as per the randomisation allocation.

However, there may be cases where this is inappropriate, such as where there is a decision to transition from active treatment to palliation. In this context, we would classify this as a 'contraindication to awake prone positioning', allowing you to stop the intervention in line with the protocol.

Can the participant carry on proning after 5 days?

Yes.

Ongoing use of the awake prone position after day 5 (120 hours from randomisation) is at the discretion of the clinical team in collaboration with the participant. Where this is done, the case report form collects information on duration of awake prone positioning after day 5.

Data Collection

Whilst randomising, how do I select the correct 'Care Setting' for the patient?

For the study we have split care setting up into 3 main types which are defined as:

- Critical care = A unit (intensive care unit/high dependency unit/combined unit) that delivers level two or three care.
- Respiratory support unit = A specialised respiratory unit that provides enhanced care and monitoring for patients with respiratory failure, beyond that expected for a routine ward environment. This likely includes the ability to deliver high-flow nasal oxygen, CPAP or non-invasive ventilation.
- Ward / Other = general acute care area, including acute medical units, respiratory wards and surgical wards, or any other care setting

What do I need to complete if a patient dies?

If a patient dies whilst in hospital and the event is not on the Exemption List or the pre-specified complications list, complete the Serious Adverse Event Form immediately; this must be entered within 24 hours of being made aware of the event.

In addition, complete the Notification of Death Form immediately; this will ensure the CTU team do not send questionnaires out to the participant.

Complete the Critical Care Events Form and Ventilation Events Form within the core part of the database.

Follow Up

Who co-ordinates follow-up after critical care discharge?

Warwick CTU will co-ordinate all follow-up after critical care discharge. We will contact you for patients' survival status prior to sending out their follow up questionnaires. These questionnaires cannot be sent until survival status is confirmed so it is important you respond promptly to these survival status requests.