RECOVERY-RS
RESPIRATORY SUPPORT

WARWICK

RECOVERY-RS Respiratory Support: Respiratory Strategies in COVID-19; CPAP, High-flow, and standard care

Site Initiation Visit

V7.0 05 Feb 2021

Acknowledgements

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intensive care society
50 YEARS
proud to be the voice of critical care since 1970

QUEEN'S UNIVERSITY BELFAST
ESTP1845

NHS
University Hospitals Birmingham
NHS Foundation Trust

SUPPORTED BY
NIHR | National Institute for Health Research

General Study Information

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❖ Chief Investigator	Prof. Gavin Perkins & Prof. Danny McAuley
❖ Sponsor	University of Warwick
❖ Funder	National Institute for Health Research
❖ Co-ordinating Centre	Warwick Clinical Trials Unit
❖ Contact	RECOVERY-RS@warwick.ac.uk
❖ Website	www.warwick.ac.uk/recovery-rs

NIHR | National Institute for Health Research

RECOVERY-RS is listed as a priority UPH study:
https://www.nihr.ac.uk/covid-studies/study-detail.htm?entryId=282338

Background and need for trial

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- COVID-19: wide spectrum of clinical severity, ranging from asymptomatic to critically illness
- Acute hypoxaemic respiratory failure- important complication
- Uncertainty as to best strategy to reduce need for tracheal intubation in COVID-19

Variability in practice

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- Uncertainty regarding optimum clinical management of COVID-19 patients with acute hypoxaemic respiratory failure
- Clinical guidelines- variability across national and international guidelines
- Practices across UK hospitals include:
  - CPAP and/or HFNO
  - Oxygen only pathway- low threshold for intubation
  - Oxygen only pathway- higher threshold for intubation

Need for trial

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- COVID-19
  - New disease; different physiology
  - Clinical trials have been an essential part of improving COVID-19 outcomes (e.g. dexamethasone)
  - Evidence base for respiratory management lacking
  - Benefits and potential risks for each respiratory support strategy
  - **BUT**….no high quality evidence base for guiding clinical practice

- Urgent need for trial of High Flow Nasal Oxygen (HFNO) vs Continuous Positive Airway Pressure (CPAP) vs standard care oxygen

Aim of trial

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To determine if CPAP or HFNO is clinically effective compared to standard care (excluding CPAP or HFNO) in relation to intubation and mortality in patients with confirmed or suspected COVID-19

Design

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- *Adaptive*, randomised controlled, open label trial comparing CPAP vs HFNO vs standard care*
- Multi-centre 70+ NHS hospitals or purpose built-hospitals
- Adult, critically ill patients, with suspected or confirmed, COVID-19
- Overall maximum recruitment target **4002 patients over 12 months**

* Uncertainty/equipoise between UK and ANZICS guidance regarding the use of CPAP and HFNO

Outcomes

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Primary outcome

Intubation or mortality within 30 days

Secondary outcomes

- Intubation rates
- Duration of invasive ventilation
- Time to intubation
- Time to death (mortality)
- Mortality in critical care (level 2/3)
- Mortality in hospital stay
- Mortality at 30 days
- Admission to ICU
- Length of stay in critical care (level 2/3)
- Length of stay in hospital
- AEs/SAEs

Eligibility

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Inclusion criteria

- ✓ Adults ≥ 18 years
- ✓ Hospital inpatient with suspected or proven COVID-19
- ✓ FiO_2 ≥0.4 and SpO_2 ≤94%*
- ✓ Plan for escalation to intubation if needed

**Requirement for oxygenation should be ongoing (not transient)*

Exclusion criteria

- ✗ Planned intubation and mechanical ventilation imminent within 1 hour
- ✗ Known or clinically apparent pregnancy
- ✗ Any absolute contraindication to CPAP or HFNO
- ✗ Decision not to intubate due to ceiling of treatment or withdrawal of treatment anticipated
- ✗ Equipment for both CPAP and HFNO not available

Screening

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- Site research team attend/contact hospital clinical areas
  Treating known or suspected COVID-19 patients
- Liaise with clinical staff to identify patients
  Acute Hypoxaemic Respiratory Failure
- Doctor/nurse/research team can assess and confirm eligibility prior to randomisation – complete eligibility form
- Justification for patient meeting all eligibility criteria
  Clearly documented in the patient's medical notes

Randomisation

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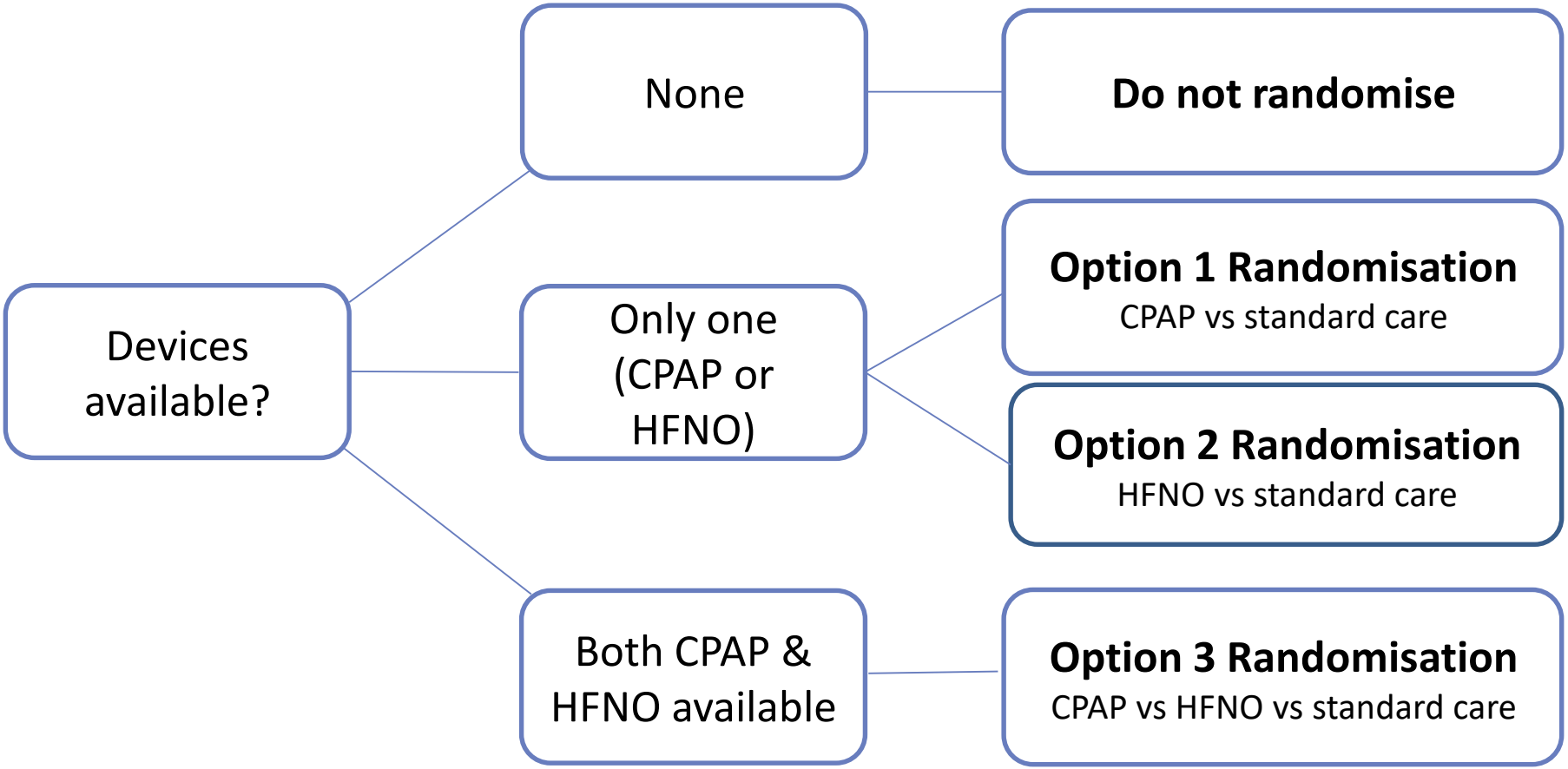
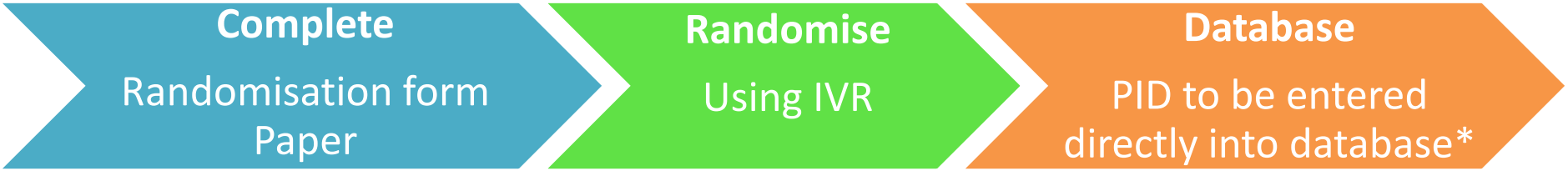
Check availability of CPAP and/or HFNO device prior to randomisation (any brand of device can be used)



Randomisation

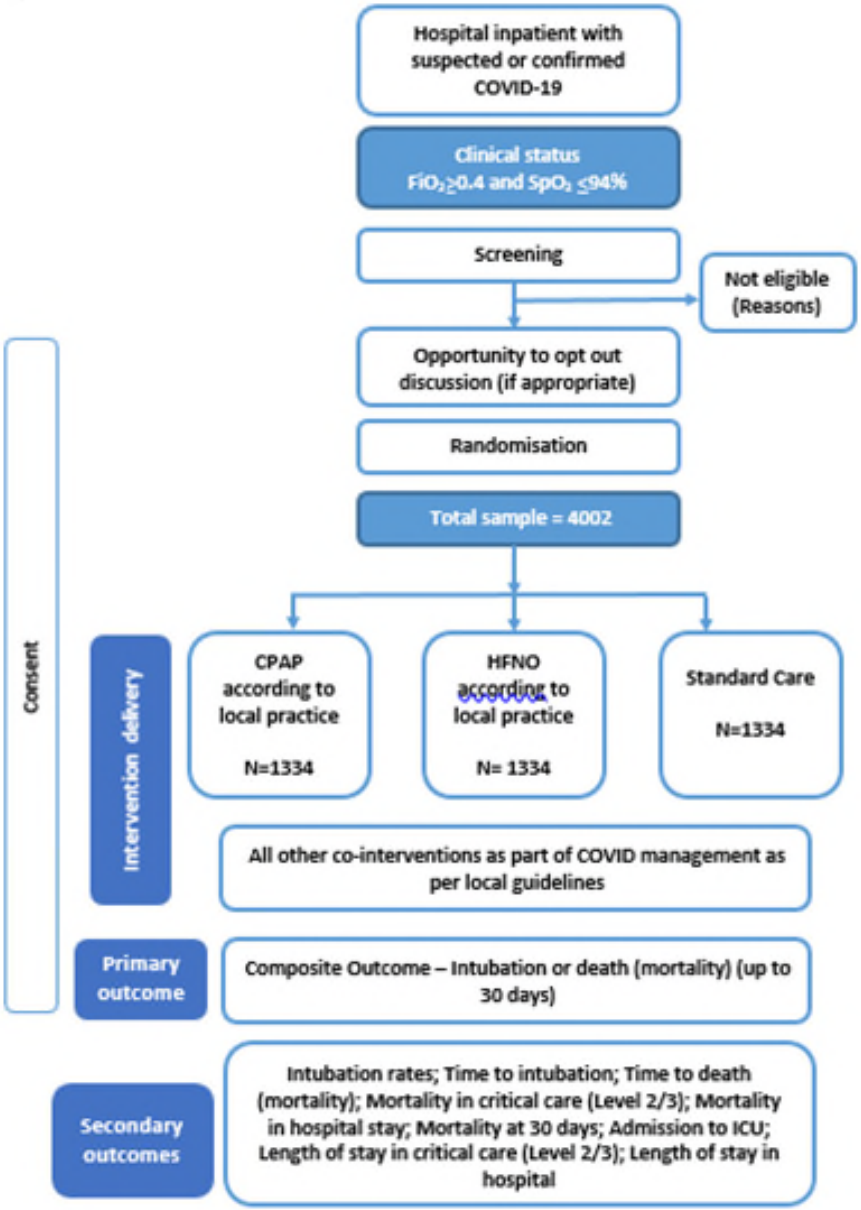
- Patients will be randomised to a 1:1:1 ratio
- Interactive Voice Response (IVR) system (24/7 service)
  Call 02476 109940
- PIN access to be provided by email following ‘green light’ to begin recruitment – generic username for each site



**PID is redacted on entry*

- Completed paper form to be filed in ISF

Trial Flow Diagram



Trial Interventions

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Ensure clear plans and safety measures in place in relation to oxygen usage and flow

1. Continuous Positive Airway Pressure	CPAP will be administered according to local protocol/guidelines. Details of initial settings (PEEP and FiO_2) will be recorded on the CRF
2. High Flow Nasal Oxygen	HFNO will be administered according to local protocol/guidelines
3. Standard care	Standard care will comprise regular oxygen therapy according to local protocol/guidelines, and exclude use of CPAP and HFNO

Administration of all interventions are left to clinical discretion for management

Trial intervention crossover

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Following scenarios are **exempt** from crossover of trial intervention and **should not** be reported on the e-CRF:

- Up to 6 hours of continuous use of crossover intervention
- Breaks for eating and drinking
- Bridge to intubation to stabilise the patient
- Palliative care purposes

- ❑ Crossover may lead to poorer prognostic outcomes and delay intubation
- ❑ We do not know whether crossover causes harm
- ❑ Crossover will affect the data integrity and inflate sample size
- ❑ Patients consent should be honoured by sticking to randomised intervention
- ❑ Encourage communication between clinical teams to avoid crossover and raise awareness of allocated arm

Trial Interventions

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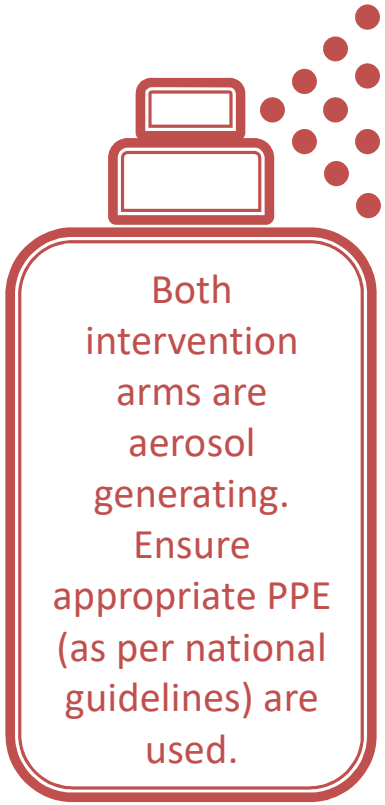
Ensure clear plans and safety measures in place in relation to oxygen usage and flow

1. Continuous Positive Airway Pressure

2. High Flow Nasal Oxygen



Both intervention arms are aerosol generating. Ensure appropriate PPE (as per national guidelines) are used.

Administration of all interventions are left to clinical discretion for management

Safety Alert: High-Flow Oxygen

Dr Ganesh Suntharalingam - President, Intensive Care Society

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Urgently ensure liaison between clinicians and hospital oxygen engineering teams to ascertain:

- the maximum flow rate from your VIE
- any additional limitations to oxygen delivery owing to pipework architecture
- calculate the maximum number of patients who can be treated with high flow devices such as wall CPAP and communication of this to the relevant clinical teams
- undertake a daily count of the number of high-flow systems where the potential oxygen flow rate exceeds 10 L/min (this will include most wall CPAP systems, High Flow Nasal Oxygen (HFNO), some non-invasive ventilators used in acute settings, and many ventilators used in critical care units or operating theatres)
- implement safety measures to prevent accidental O2 system failure (such as limiting the number of these devices available for clinical use)

"low oxygen pressure alarms" = indication of approaching flow limitation
TAKE URGENT ACTION: Review usage, reduce demand, escalate for engineering assistance

Consent process (England, Wales and Northern Ireland)

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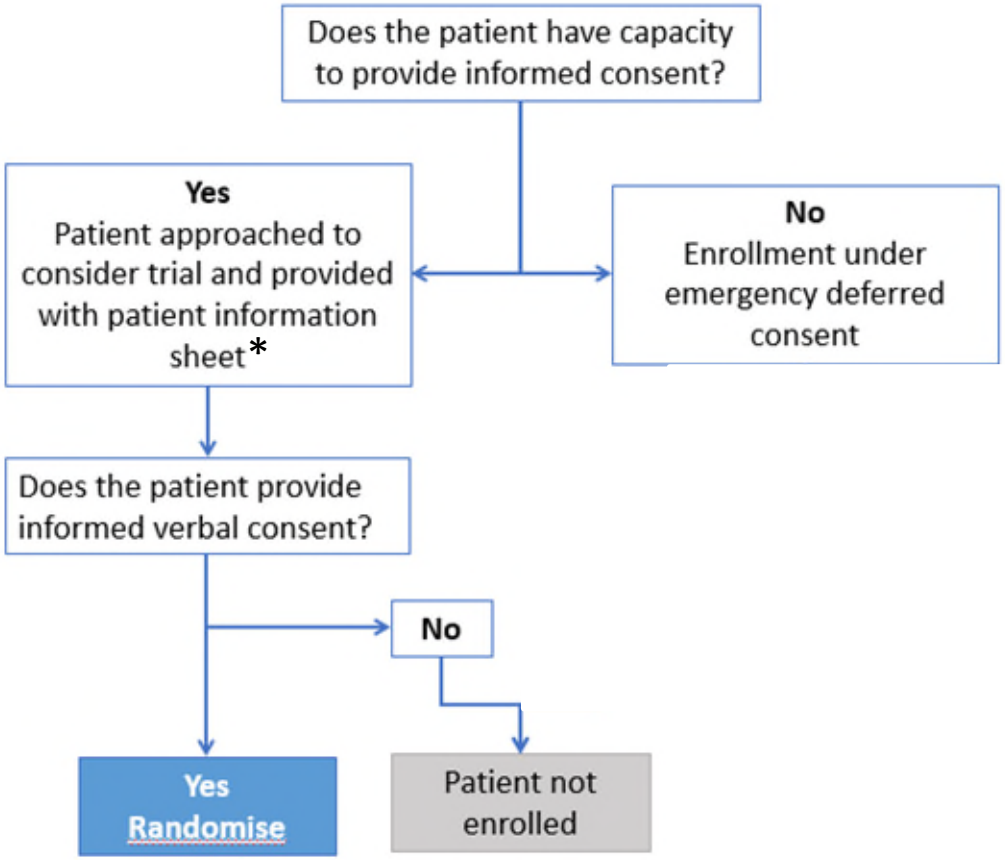
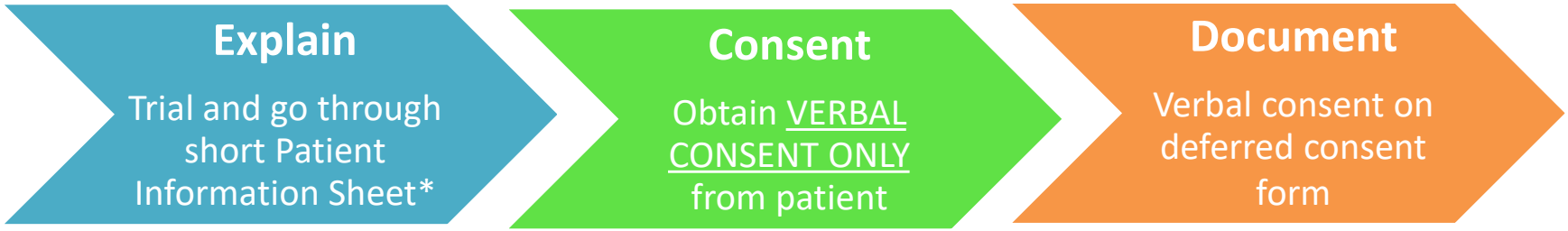


*** Ensure the patient is informed if only one intervention (CPAP or HFNO) is available**

Deferred consent (England, Wales and Northern Ireland)

- If patient regains capacity, they should be given the option to consent/withdraw



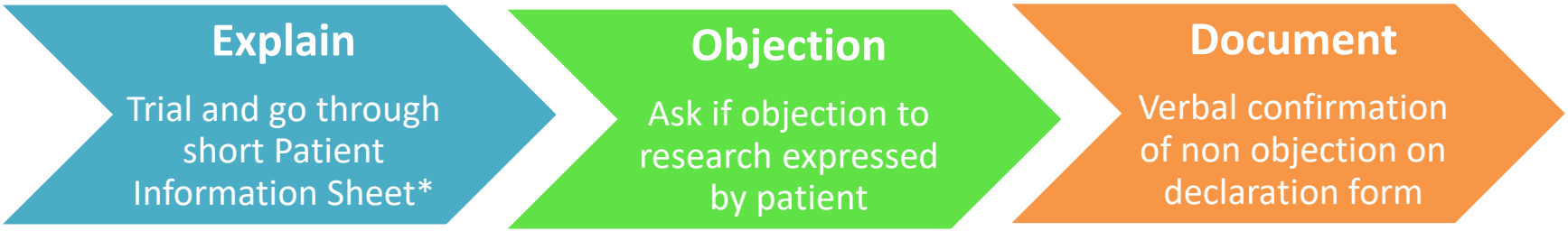
* Long version available on website if requested

- Documents including the PIS can be found on the website

- If consent not obtained before patient discharged/transferred, attempt to contact patient or their consultee (if patient lacks mental capacity) by telephone to seek verbal agreement (up to 3 attempts).
- Provide details of website which contains PIS to download (www.warwick.ac.uk/recovery-rs/patients)

Consultee opinion (England, Wales and Northern Ireland)

- If patient does not re-gain capacity by hospital discharge, approach a personal or professional consultee
- Personal consultee before professional consultee, if there is one available



* Long version available on website if requested

- Documents available on website under Patient Tab

Deferred Consent

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The deferred consent process, including assessment of capacity, will be undertaken by a member of the team delivering the trial at the hospital (e.g. doctor, nurse, research practitioner)

Personal Consultee

Contact by telephone

Documents available on website

A person who is:

- engaged in caring for the participant (not professionally or for payment) or is interested in his/her welfare, and
- is prepared to be consulted

Professional Consultee

Ordinarily registered medical practitioner who has no connection with the trial and is willing to be consulted

Consent process (Scotland)

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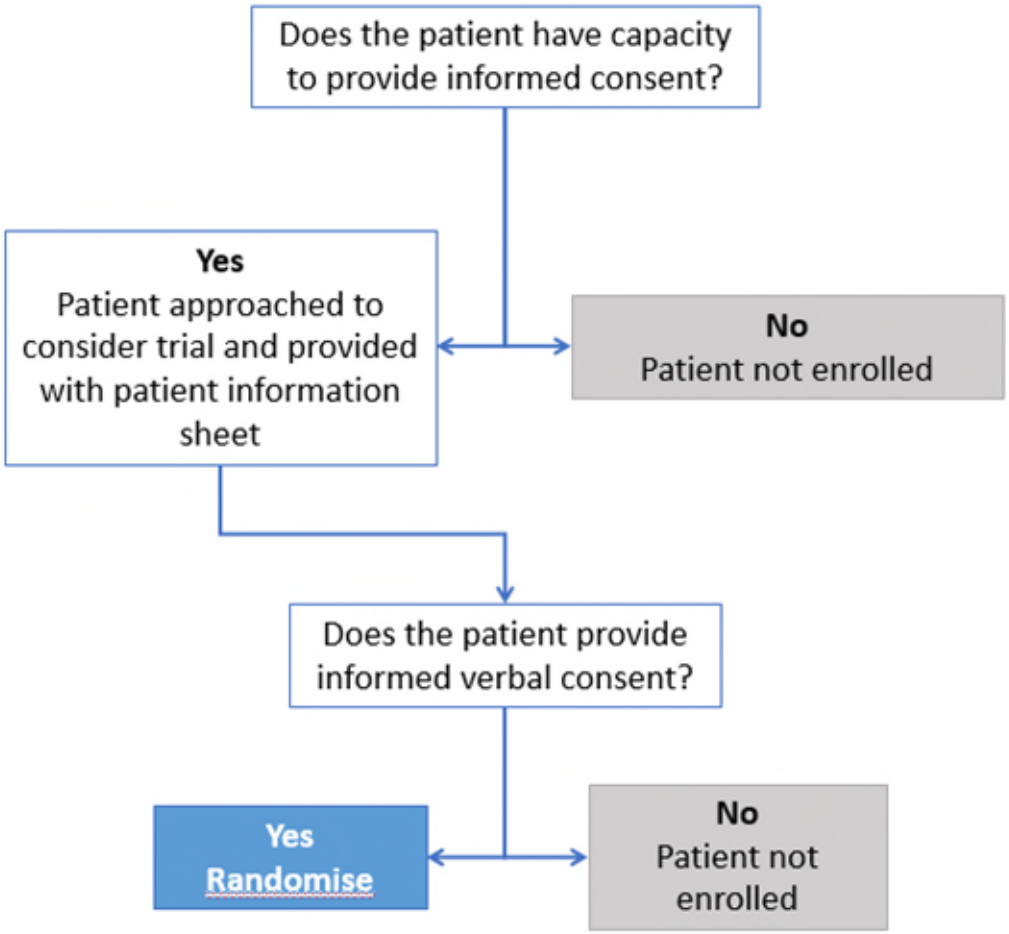

Ensure the patient is informed if only one intervention (CPAP or HFNO) is available

Consent process (Scotland)

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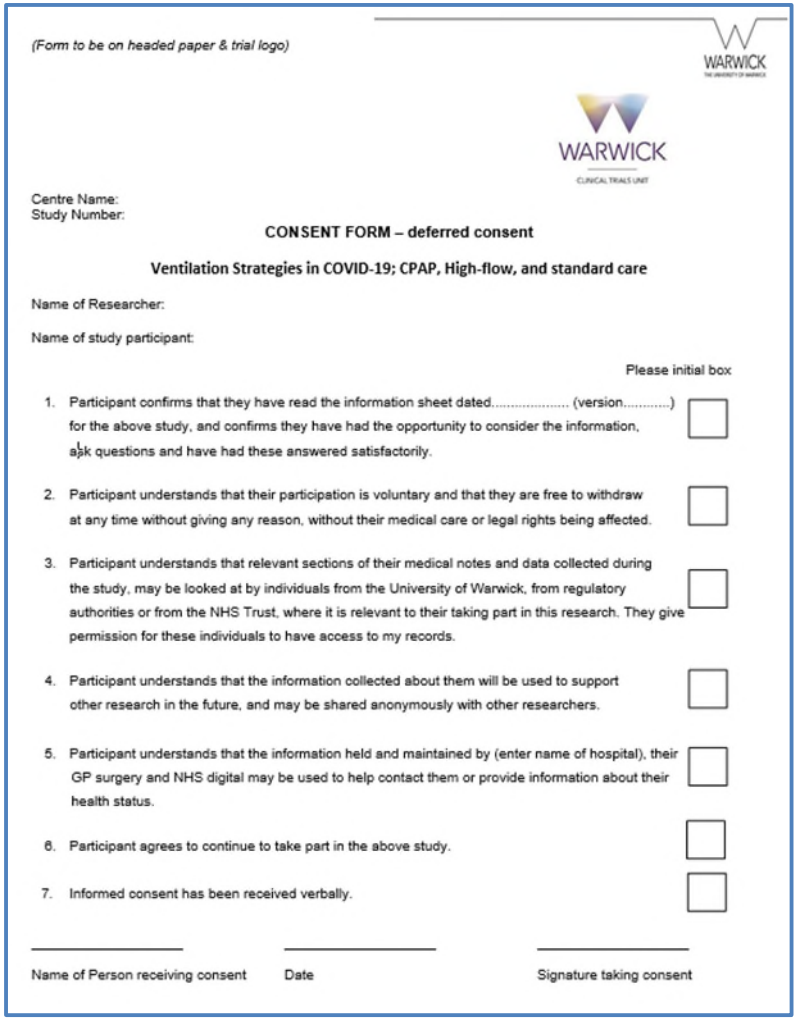
- For patients that lack capacity, it is not practical or appropriate to consult a guardian/welfare attorney prior to enrolment without placing the potential participant at risk of harm from delaying treatment.

- These processes will also not be feasible or safe to undertake in order to minimise risk of viral transmission to those involved.

- Significant limitations have been placed on the visitation of COVID-19 patients and therefore a guardian is unlikely to be immediately be available, and to attempt contact via telephone will delay treatment. **Therefore these patients will not be entered into the study as Scottish regulation do not allow emergency deferred consent.**

Consent process

- Consent should be received **verbally** from both patients and consultees to reduce risk of infection transmission
- **Only** person receiving consent should sign the consent/declaration form
- Three signed copies:
  - One for ISF
  - One for patient/consultee
  - One for medical notes
- **Do not** send copies of consent forms to Warwick CTU. They should be stored securely at site
- Consent should be documented in the patient's medical notes



(Form to be on headed paper & trial logo)

Centre Name:
Study Number:

CONSENT FORM – deferred consent

Ventilation Strategies in COVID-19; CPAP, High-flow, and standard care

Name of Researcher:

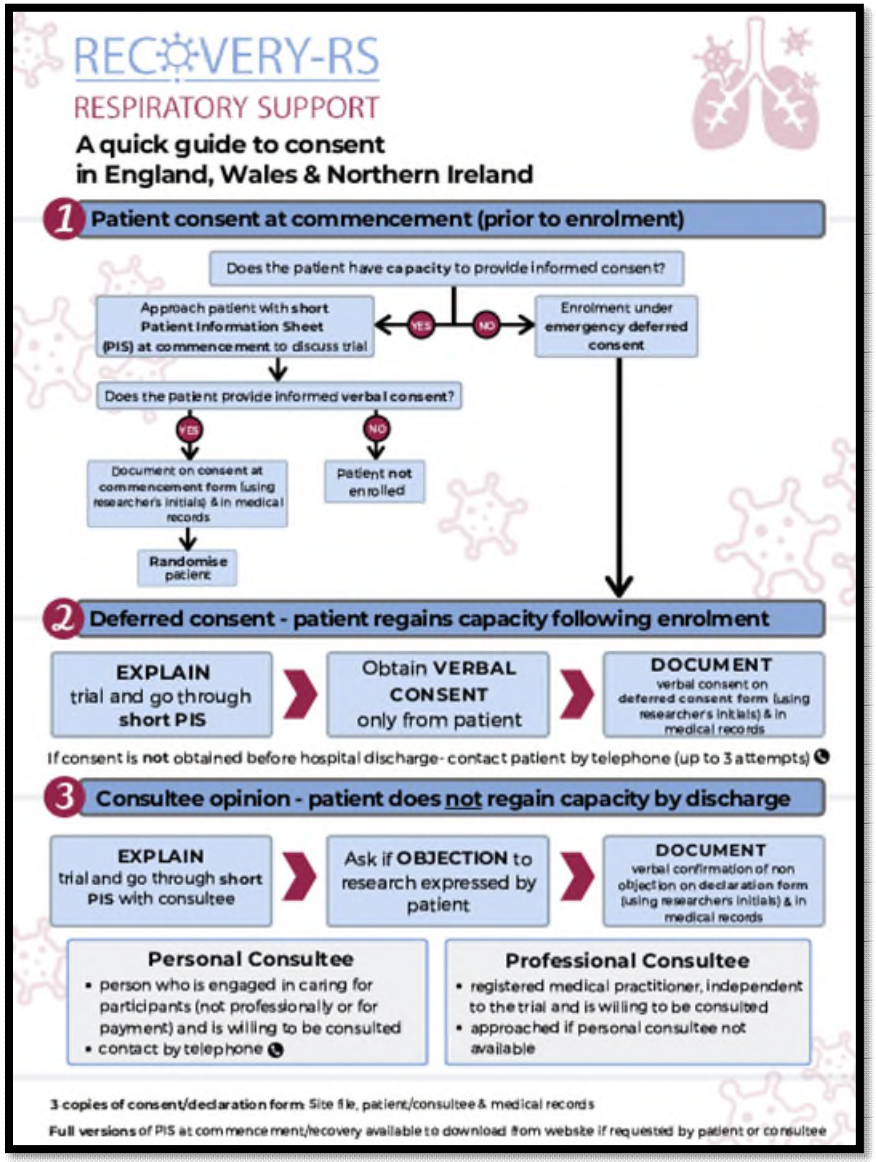
Name of study participant:

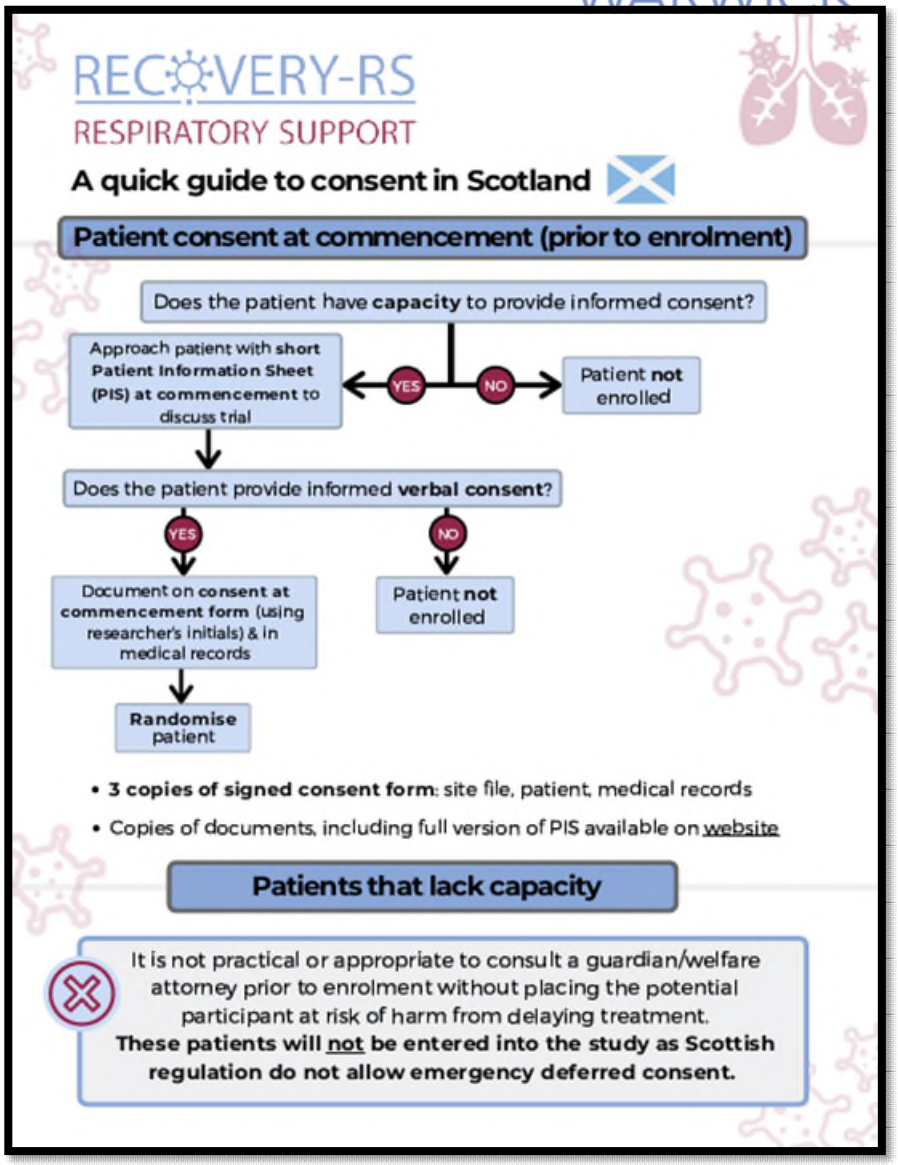
Please initial box

1. Participant confirms that they have read the information sheet dated..... (version.....) for the above study, and confirms they have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. Participant understands that their participation is voluntary and that they are free to withdraw at any time without giving any reason, without their medical care or legal rights being affected. ☐
3. Participant understands that relevant sections of their medical notes and data collected during the study, may be looked at by individuals from the University of Warwick, from regulatory authorities or from the NHS Trust, where it is relevant to their taking part in this research. They give permission for these individuals to have access to my records. ☐
4. Participant understands that the information collected about them will be used to support other research in the future, and may be shared anonymously with other researchers. ☐
5. Participant understands that the information held and maintained by (enter name of hospital), their GP surgery and NHS digital may be used to help contact them or provide information about their health status. ☐
6. Participant agrees to continue to take part in the above study. ☐
7. Informed consent has been received verbally. ☐

Name of Person receiving consent | Date | Signature taking consent

Consent process





Co-enrolment

Co-enrolment will be reviewed on a case-by-case basis in accordance with NIHR-supported co-enrolment guidelines

We will maintain a list of trials we are co-enrolling with on the trial website

PRINCIPLE

REALIST

RECOVERY

REMAP-CAP

PIONEER

XPORT-CoV-1001 (protocol can be found here)

TACTIC-R

ACCORD

CATALYST

VACIRiSS

ILIAD-7

STRESS-L

BLING III

A2B

ALXN1210-COV-305

FALCON - CONDOR

Data entry / eCRF

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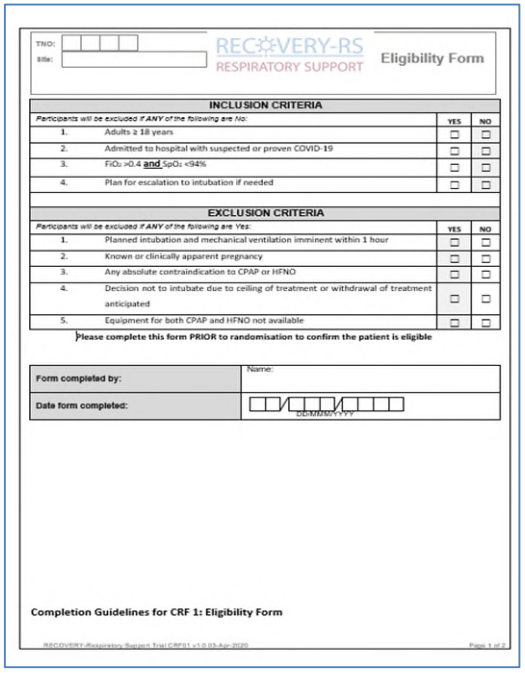
Bespoke online database - initial data to be entered:

Eligibility Form → Randomisation Form * → Baseline Form



TNO:
Site:

RECOVERY-RS RESPIRATORY SUPPORT — Eligibility Form

INCLUSION CRITERIA

Participants will be excluded if ANY of the following are No:

		YES	NO
1.	Adults ≥ 18 years	☐	☐
2.	Admitted to hospital with suspected or proven COVID-19	☐	☐
3.	FiO_2 >0.4 and SpO_2 <94%	☐	☐
4.	Plan for escalation to intubation if needed	☐	☐

EXCLUSION CRITERIA

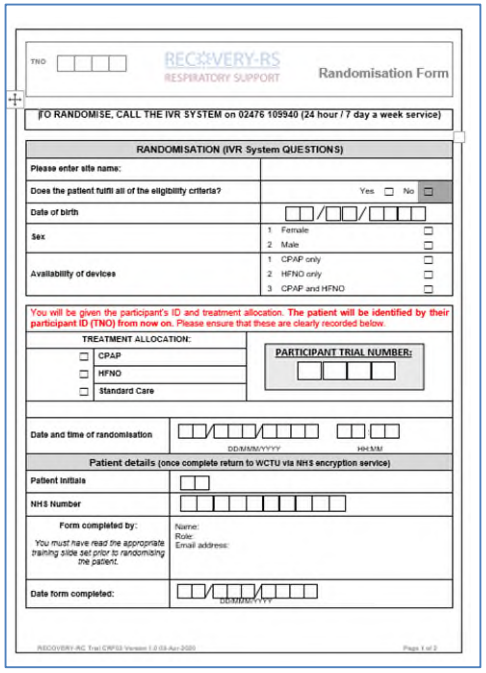
Participants will be excluded if ANY of the following are Yes:

		YES	NO
1.	Planned intubation and mechanical ventilation imminent within 1 hour	☐	☐
2.	Known or clinically apparent pregnancy	☐	☐
3.	Any absolute contraindication to CPAP or HFNO	☐	☐
4.	Decision not to intubate due to ceiling of treatment or withdrawal of treatment anticipated	☐	☐
5.	Equipment for both CPAP and HFNO not available	☐	☐

Please complete this form PRIOR to randomisation to confirm the patient is eligible

Form completed by:	Name:
Date form completed:	☐☐/☐☐☐/☐☐☐☐ DD/MMM/YYYY

Completion Guidelines for CRF 1: Eligibility Form



TNO:

RECOVERY-RS RESPIRATORY SUPPORT — Randomisation Form

TO RANDOMISE, CALL THE IVR SYSTEM on 02476 105940 (24 hour / 7 day a week service)

RANDOMISATION (IVR System QUESTIONS)

Please enter site name:	
Does the patient fulfil all of the eligibility criteria?	Yes ☐ No ☐
Date of birth	☐☐/☐☐/☐☐☐☐
Sex	1 Female ☐ 2 Male ☐
Availability of devices	1 CPAP only ☐ 2 HFNO only ☐ 3 CPAP and HFNO ☐

You will be given the participant's ID and treatment allocation. The patient will be identified by their participant ID (TNO) from now on. Please ensure that these are clearly recorded below.

TREATMENT ALLOCATION:

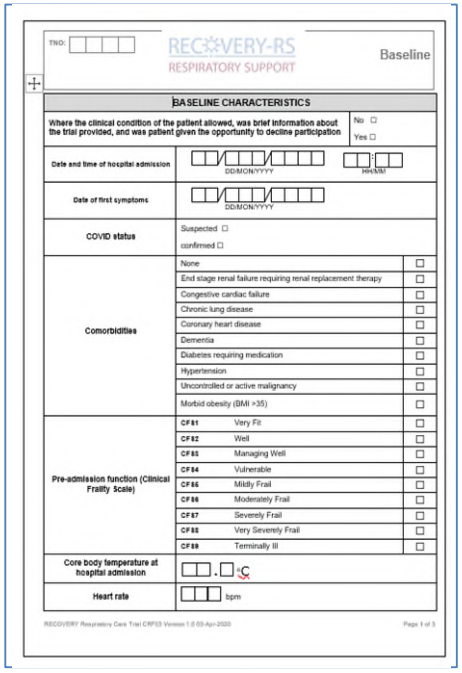
☐ CPAP
☐ HFNO
☐ Standard Care

PARTICIPANT TRIAL NUMBER: ☐☐☐☐

Date and time of randomisation	☐☐/☐☐☐/☐☐☐☐ DD/MMM/YYYY ☐☐:☐☐ HH:MM

Patient details (once complete return to WCTU via NHS encryption service)

Patient initials	☐☐
NHS Number	☐☐☐☐☐☐☐☐☐☐
Form completed by: *You must have read the appropriate training slide set prior to randomising the patient.*	Name: Role: Email address:
Date form completed:	☐☐/☐☐☐/☐☐☐☐ DD/MMM/YYYY



TNO:

RECOVERY-RS RESPIRATORY SUPPORT — Baseline

BASELINE CHARACTERISTICS

Where the clinical condition of the patient allowed, was brief information about the trial provided, and was patient given the opportunity to decline participation		No ☐ Yes ☐
Date and time of hospital admission		☐☐/☐☐☐/☐☐☐☐ DD/MON/YYYY ☐☐:☐☐ HH:MM
Date of first symptoms		☐☐/☐☐☐/☐☐☐☐ DD/MON/YYYY
COVID status		Suspected ☐ confirmed ☐
Comorbidities		None ☐
		End stage renal failure requiring renal replacement therapy ☐
		Congestive cardiac failure ☐
		Chronic lung disease ☐
		Coronary heart disease ☐
		Dementia ☐
		Diabetes requiring medication ☐
		Hypertension ☐
		Uncontrolled or active malignancy ☐
		Morbid obesity (BMI >35) ☐
Pre-admission function (Clinical Frailty Scale)	CFS1	Very Fit ☐
	CFS2	Well ☐
	CFS3	Managing Well ☐
	CFS4	Vulnerable ☐
	CFS5	Mildly Frail ☐
	CFS6	Moderately Frail ☐
	CFS7	Severely Frail ☐
	CFS8	Very Severely Frail ☐
	CFS9	Terminally Ill ☐
Core body temperature at hospital admission		☐☐.☐ °C
Heart rate		☐☐☐ bpm

* To include Personal Identifiable Data

Data entry / eCRF

Generic site user ID

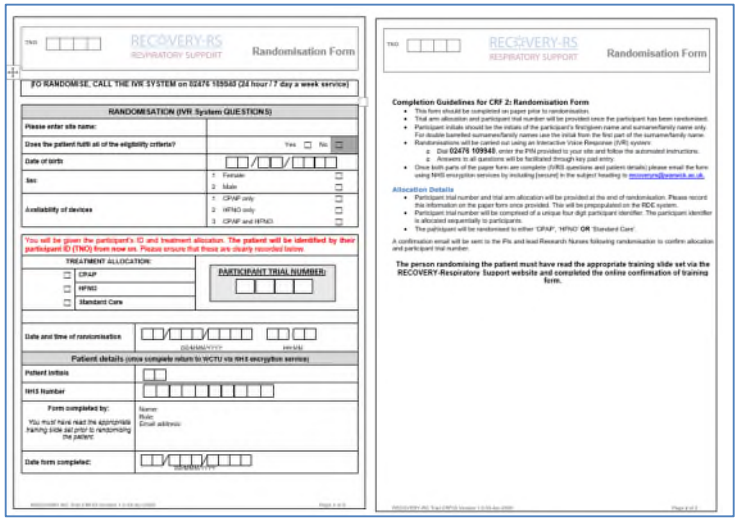
Provided by email
following 'green light' approval

Paper/Electronic

Optional whether paper CRF's
used prior to entry

Personal Identifiable Data

Collected on Randomisation CRF and entered onto the randomisation eCRF. PID will be anonymised upon data entry to allow storage



Data collection

Visit	1	2	3	4
Visit Window (No. Weeks ± No. Days)	Day 0 Baseline	Regular in-hospital reviews (at least weekly)	Day 30 (+/- 2 days)†	Hospital discharge†
Baseline data collection	✓			
Randomisation	✓			
Intervention	✓*	✓*		
Adverse events		✓	✓	✓
Survival status		✓	✓	✓
Outcome assessment			✓	✓

*- Intervention will be delivered up to point of death, decision to palliate, tracheal intubation, or clinical determination that no ongoing need

†- Participants to be followed-up to day 30 or hospital discharge, whichever comes later

Follow up

If patient still in hospital complete follow-up eCRF at **30 days post randomisation** or **hospital discharge** whichever is the later

Data Collection

- ICU/hospital admission status
- Ventilation duration
- AEs (treatment failure, need for other treatments, renal function, renal replacement therapy)
- Survival status*

*If patient discharged before day 30, trial team will obtain survival data through data linkage

Withdrawal

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Participants may be discontinued from the trial treatment and/or the trial at any time without prejudice

Please notify Warwick CTU of any withdrawals

Complete the withdrawal form on the online database

Data Collected

Data collected up until withdrawal point will automatically be used unless participant specifically requests otherwise

Follow-up

Unless a participant explicitly withdraws their consent, they will be followed-up wherever possible and data collected as per the protocol until the end of the trial

Withdrawal Options

Withdraw from trial treatment

Withdraw completely

Document

Date of withdrawal in Medical Notes

Withdrawal form

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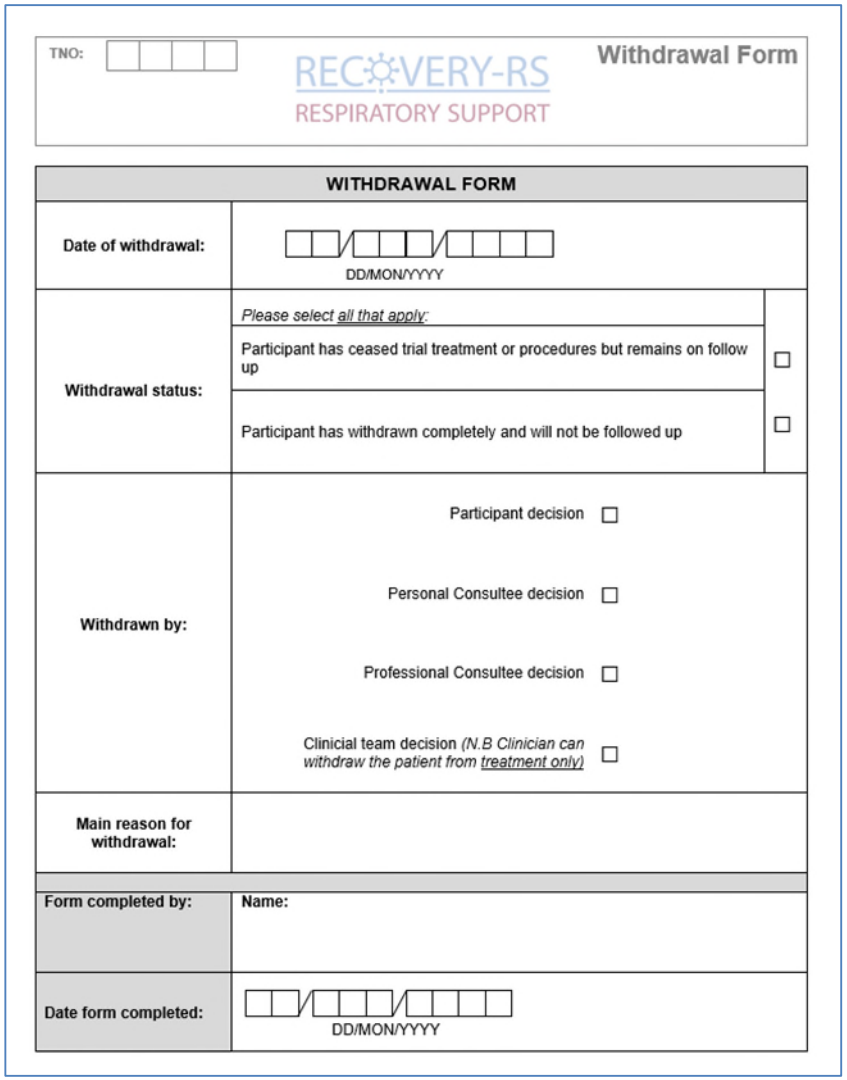

TNO: ☐☐☐☐

RECOVERY-RS
RESPIRATORY SUPPORT

Withdrawal Form

WITHDRAWAL FORM		
Date of withdrawal:	☐☐/☐☐☐/☐☐☐☐ DD/MON/YYYY	
Withdrawal status:	*Please select all that apply:*	
	Participant has ceased trial treatment or procedures but remains on follow up	☐
	Participant has withdrawn completely and will not be followed up	☐
Withdrawn by:	Participant decision	☐
	Personal Consultee decision	☐
	Professional Consultee decision	☐
	Clinicial team decision *(N.B Clinician can withdraw the patient from treatment only)*	☐
Main reason for withdrawal:		
Form completed by:	**Name:**	
Date form completed:	☐☐/☐☐☐/☐☐☐☐ DD/MON/YYYY	

Safety reporting

Only AE's listed below and **clearly related** to the use of CPAP or HFNO or **expected** to be recorded. Record AE's on the online database

The following are expected adverse events and will be recorded in the CRF; they predominantly relate to the use of CPAP, as there are minimal AEs reported for HFNO:

- **Interface intolerance due to excessive air leaks**
- **Pain**
- **Cutaneous pressure sore or pressure area**
- **Claustrophobia**
- **Oro-nasal dryness**
- **Respiratory acidosis with pH <7.25 prior to intubation**
- **Haemodynamic instability**
- **Vomiting**
- **Aspiration of gastric contents**
- **Pneumothorax**
- **Pneumomediastinum**

Safety reporting

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Only SAEs that occur from the time of randomisation, **through to and including 30 days** after cessation of trial intervention, must be reported to WCTU

Scan and email completed SAE forms to WCTUQA@warwick.ac.uk **within 24 hours, or as soon as is practicable,** of becoming aware of the event

Events that commonly occur in this population and collected as trial outcomes do not need to be reported as SAEs.

Events that do **NOT** need to be reported as SAEs:

- Death
- Organ failure
- Pneumonia
- Intubation
- Tracheostomy

Events that are related to the patient's underlying disease or condition should **not** be reported.

SAE forms

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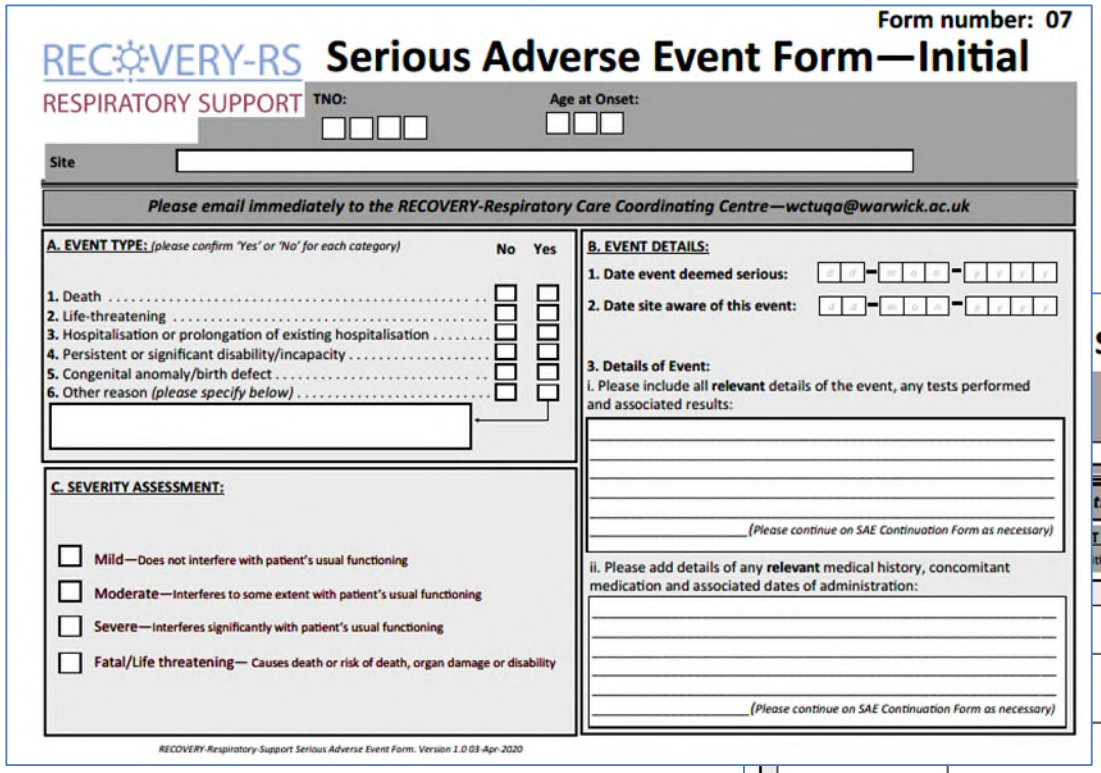


Form number: 07

RECOVERY-RS RESPIRATORY SUPPORT

Serious Adverse Event Form—Initial

TNO: ☐☐☐☐ Age at Onset: ☐☐☐

Site

Please email immediately to the RECOVERY-Respiratory Care Coordinating Centre—wctuqa@warwick.ac.uk

A. EVENT TYPE: *(please confirm 'Yes' or 'No' for each category)*

	No	Yes
1. Death	☐	☐
2. Life-threatening	☐	☐
3. Hospitalisation or prolongation of existing hospitalisation	☐	☐
4. Persistent or significant disability/incapacity	☐	☐
5. Congenital anomaly/birth defect	☐	☐
6. Other reason *(please specify below)*	☐	☐

B. EVENT DETAILS:

1. Date event deemed serious: d d - m o n - y y y y
2. Date site aware of this event: d d - m o n - y y y y

3. Details of Event:

i. Please include all **relevant** details of the event, any tests performed and associated results:

(Please continue on SAE Continuation Form as necessary)

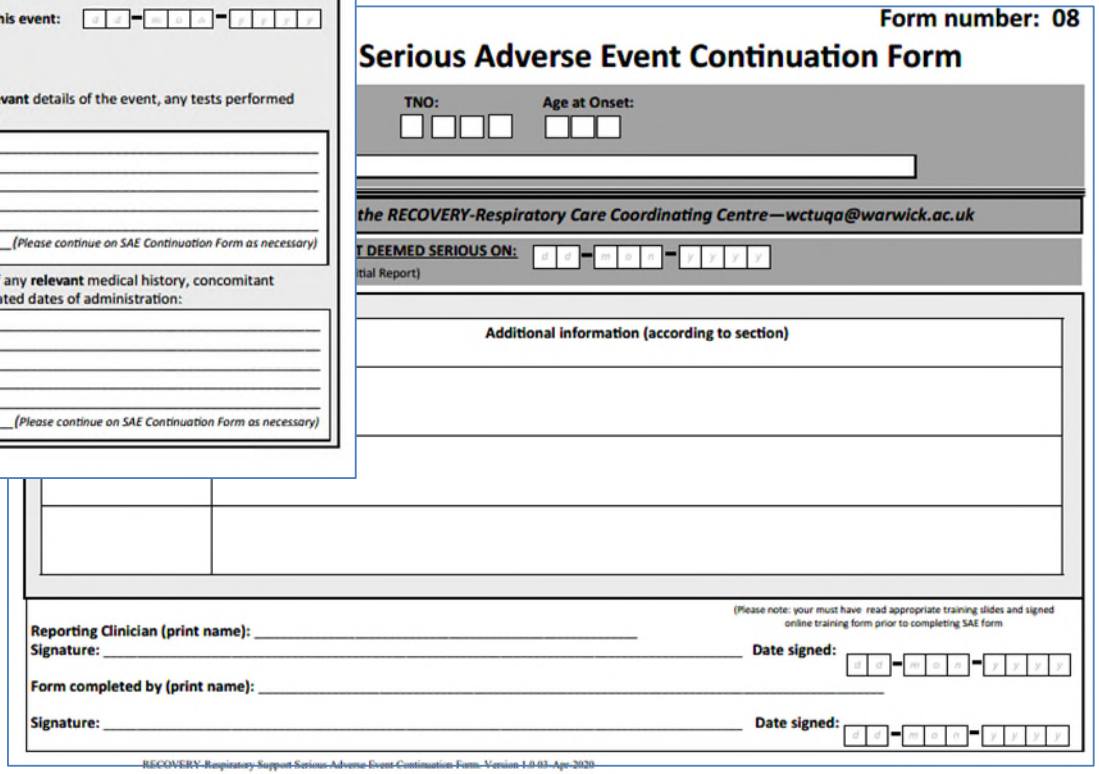
ii. Please add details of any **relevant** medical history, concomitant medication and associated dates of administration:

(Please continue on SAE Continuation Form as necessary)

C. SEVERITY ASSESSMENT:

- ☐ Mild—Does not interfere with patient's usual functioning
- ☐ Moderate—Interferes to some extent with patient's usual functioning
- ☐ Severe—Interferes significantly with patient's usual functioning
- ☐ Fatal/Life threatening— Causes death or risk of death, organ damage or disability

RECOVERY-Respiratory-Support Serious Adverse Event Form. Version 1.0 03-Apr-2020



Form number: 08

Serious Adverse Event Continuation Form

TNO: ☐☐☐☐ Age at Onset: ☐☐☐

the RECOVERY-Respiratory Care Coordinating Centre—wctuqa@warwick.ac.uk

T DEEMED SERIOUS ON: d d - m o n - y y y y
tial Report)

Additional information (according to section)

(Please note: your must have read appropriate training slides and signed online training form prior to completing SAE form

Reporting Clinician (print name): _____

Signature: _____ Date signed: d d - m o n - y y y y

Form completed by (print name): _____

Signature: _____ Date signed: d d - m o n - y y y y

~~RECOVERY-Respiratory-Support-Serious-Adverse-Event-Continuation-Form. Version 1.0 03-Apr-2020~~

Non-compliance

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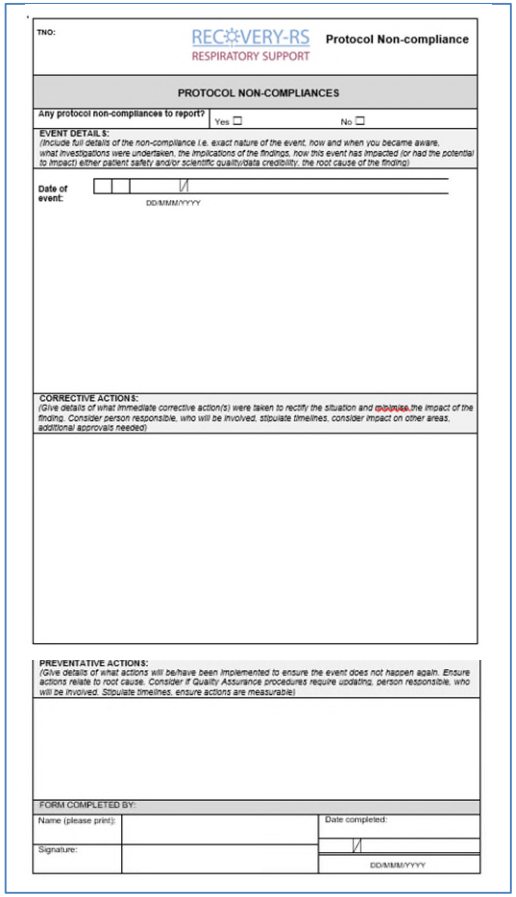
Report any non-compliances immediately to WCTU straight onto online database (within 24 hours of becoming aware)

Examples of non-compliances:

- Patient doesn't receive intervention they are randomised to
- Patient is ineligible
- Staff member not completed trial training on website
- No active effort to follow up patients to obtain retrospective consent if they regain capacity or to approach consultee for consent
- Patient requests withdrawal of data but site does not inform Warwick CTU



TNO:

RECOVERY-RS RESPIRATORY SUPPORT — Protocol Non-compliance

PROTOCOL NON-COMPLIANCES

Any protocol non-compliances to report? Yes ☐ No ☐

EVENT DETAILS:
(Include full details of the non-compliance i.e. exact nature of the event, how and when you became aware, what investigations were undertaken, the implications of the findings, how this event has impacted (or had the potential to impact) either patient safety and/or scientific quality/data credibility; the root cause of the finding)

Date of event: DD/MM/YYYY

CORRECTIVE ACTIONS:
(Give details of what immediate corrective action(s) were taken to rectify the situation and minimise the impact of the finding. Consider person responsible, who will be involved, stipulate timelines, consider impact on other areas, additional approvals needed)

PREVENTATIVE ACTIONS:
(Give details of what actions will be/have been implemented to ensure the event does not happen again. Ensure actions relate to root cause. Consider if Quality Assurance procedures require updating, person responsible, who will be involved. Stipulate timelines, ensure actions are measurable)

FORM COMPLETED BY:

Name (please print):		Date completed:
Signature:		DD/MM/YYYY

Training requirements QA

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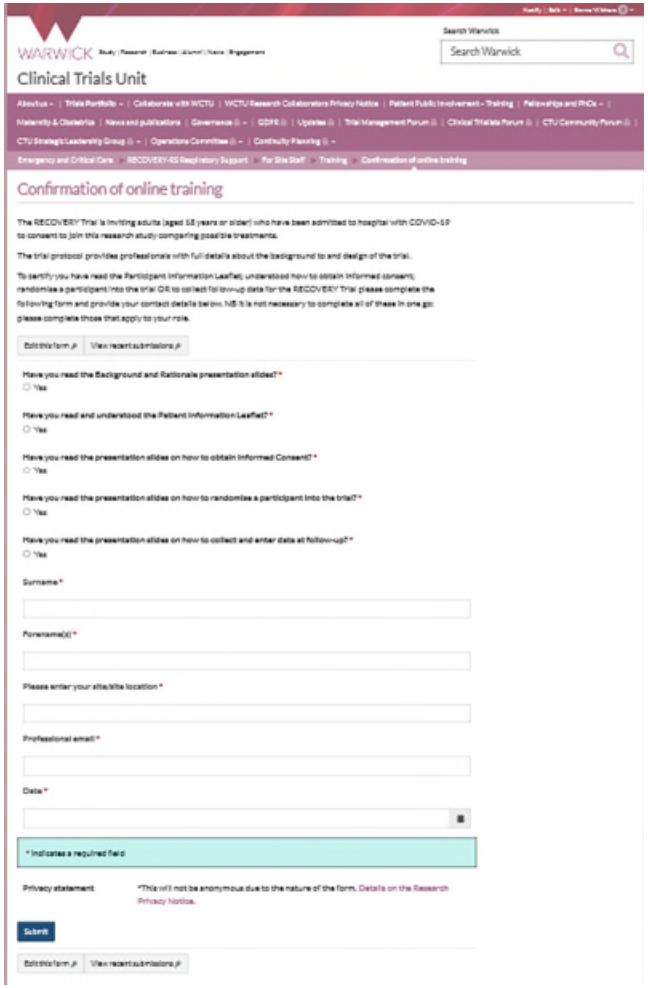
- Training is available on the trial website
- As a **minimum** the PI of the site must complete and sign off all training modules on the website
- PI to ensure that staff (e.g. doctor, nurse, research practitioner) have the appropriate knowledge and understanding of trial
- All training should be recorded on the Confirmation of Online Training Form
- Optional GCP training available on website
- There is no need for the PI to provide a CV and GCP certificate.



Study oversight

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Investigator Site File (ISF)

Available on website

Monitoring

Central monitoring approach will be developed that will take into account the challenging circumstances and staff pressures

Close Out

- Resolve any outstanding queries
- Collect any outstanding data
- Ongoing responsibilities
- Site to archive trial documentation and data (at least 10 years)

Aide memoirs – available on website

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RESPIRATORY SUPPORT

INCLUSION CRITERIA

✓Adults ≥ 18 years

✓2. Hospital inpatient with suspected or proven COVID-19

✓FiO_2 ≥0.4 **and** SpO_2 ≤94%

✓Plan for escalation to intubation if needed

EXCLUSION CRITERIA

X Planned intubation and mechanical ventilation imminent within 1 hour

X Known or clinically apparent pregnancy

X Any absolute contraindication to CPAP or HFNO

X Decision not to intubate due to ceiling of treatment or withdrawal of TREATMENT anticipated

X Equipment for both CPAP and HFNO not available

If you have any questions:

Ask: Your local Principal Investigator
Visit: www.warwick.ac.uk/recovery-rs
Email: RECOVERY-RS@warwick.ac.uk
If urgent call: *<Insert trial Tel Number>*

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Are you looking after a patient aged **>18 years**?
Who has **suspected** or **proven COVID-19**?
Who has a clinical status **FiO_2 ≥0.4 and SpO_2 ≤94%**
Is there a plan for escalation to intubation if needed?

If you answered **YES** to all of the above please consider the **RECOVERY Respiratory Support Trial**

RECOVERY Respiratory Support is looking at ventilation strategies CPAP, High-flow and standard care.

If you think you have an eligible patient please contact your local research team:

<INSERT NAME>
<INSERT CONTACT DETAILS>

If you have any questions:

Ask: Your local Principal Investigator *<INSERT NAME & CONTACT DETAILS>*
Visit: www.warwick.ac.uk/recovery-rs
Email: RECOVERY-RS@warwick.ac.uk
If urgent call: *<Insert trial Tel Number>*

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RECOVERY-RS
RESPIRATORY SUPPORT

RECOVERY-RS SAE Reporting Process working instruction

The purpose of this working instruction document is to provide guidance on the reporting process of Serious Adverse Events (SAE) for the RECOVERY-RS trial. All SAE's are processed in accordance with Warwick CTU SOP 17 (part 1).

Principal Investigator (PI) or delegate identifies Adverse Event (AE)
PI or delegate performs seriousness assessment on AE
PI or delegate deems event fulfills serious reporting criteria as per GCP and protocol requirements
PI or delegate performs causality assessment
PI or delegate reports to Warwick CTU QA team (WCTUQA@warwick.ac.uk) as per method outlined in protocol within 24 hours of date aware or as soon as practically possible
Warwick CTU QA team receive SAE report via email. RECOVERY-RS trial team forward copy of report if QA have not initially received it
Warwick CTU QA team log SAE and perform initial triage checks and forward to RECOVERY-RS trial team
RECOVERY-RS Trial Manager (TM) or delegate assign SAE reference number and enter details on SAE log
TM or delegate review form completedness and query any key missing information with site. Relevant query correspondence saved in section 12.1 of TMF.
TM or delegate sends SAE report to the Chief Investigator (CI) as soon as possible
CI performs independent causality and expectedness assessment to confirm event classification
If event deemed related and unexpected event will be reported to sponsor and REC as soon as possible to align with Warwick CTU SOP 17 (part 1)
CI signs off SAE form. If event ongoing, TM or delegate requests follow-up SAE form from investigator site
CI signs of follow-up SAE form if required and TM sends final copy to Investigator Site, Warwick CTU QA team and files in Trial Master File
SAE reviewed at monthly TMG alongside cumulative safety information to review trends in TMG reports saved in section 9.2 of TMF. Discussion regarding SAE events found in TMG minutes saved in section 9.2 of TMF.

Investigator site
Warwick CTU QA
RECOVERY-RS Trial Team and Chief Investigator

Version 1.1 03.04.20 Page 1 of 1

RECOVERY-RS
RESPIRATORY SUPPORT

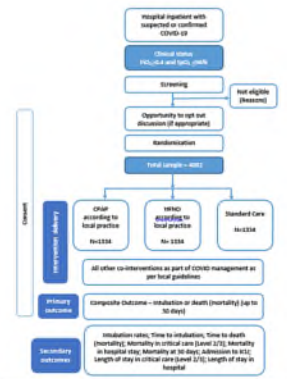
RECOVERY-RS Trial Participant Checklist

No.	Task	Guidance	Done
1	**Screen patient**	• Patient is >18 years old, has suspected or proven COVID-19, clinical status is FiO_2 ≥0.4 and SpO_2 ≤94% and there is a plan for escalation to intubation if needed. • Update patient's medical notes to document screening process and to confirm eligibility.	☐
2	**Check availability of devices**	• Check availability of any brand CPAP and HFNO device prior to randomisation (any brand can be used). • If only 1 device is available, continue with randomisation. • If no device is available = **do not randomise.**	☐
3	**Does the patient have mental capacity to provide information sheet and obtain consent?**	• If yes, provide written information sheet to patient and obtain verbal consent. Only person obtaining consent will sign consent form. • (SITES IN ENGLAND, WALES & NORTHERN IRELAND ONLY) If no, proceed with randomising patient as urgent treatment needs to be given without delay. Clearly document consent process in patient's	☐
4	**Complete paper eligibility form**	• The person confirming eligibility must have read the appropriate training slide set via the RECOVERY-RS website and completed the online confirmation of training form.	☐
5	**Complete paper randomisation form**	• The person randomising the patient must have read the appropriate training slide set via the RECOVERY-RS website and completed the online confirmation of training form.	☐
6	**Randomise patient**	• Dial 02476 109940 and enter the PIN provided to your site to randomise patient via automated 24/7 IVR system.	☐
7	**Administer intervention**	• CPAP or HFNO will be administered according to local protocol/guidelines. • Standard care will comprise regular oxygen therapy according to local protocol/guidelines and exclude use of CPAP and HFNO. • Intervention will be delivered up to point of death, decision to palliate, tracheal intubation, or clinical determination that no ongoing need.	☐
8	**Complete Randomisation form on database**	• The person randomising the patient must have read the appropriate training slide set via the RECOVERY-RS website and completed the online confirmation of training form.	☐
8	**Complete Baseline form on database**	• The person collecting data must have read the appropriate training slide set via the RECOVERY-RS website and completed the online confirmation of training form.	☐
9	**Retrospective consent (SITES IN ENGLAND, WALES & NORTHERN IRELAND ONLY)**	• If patient regains capacity, obtain verbal informed consent from patient. • If patient does not regain capacity before hospital discharge, approach personal or professional consultee for deferred consent. • If consent not obtained before patient discharged/transferred, attempt to contact patient or their consultee (if patient lacks mental capacity) by telephone to seek verbal agreement (up to 3 attempts).	☐
10	**Data collection**	• Perform regular in-hospital reviews (at least weekly) • Complete data collection CRF on database at Day 30 or hospital discharge, whichever comes later.	☐ ☐
11	**Safety Reporting** *(if applicable)*	• Record adverse events clearly related to the use of CPAP or HFNO or expected on the CRF up until day 30 or hospital discharge, whichever comes later • Report Serious adverse events on paper CRF to Warwick CTU within 24 hours of becoming aware of the event.	☐
12	**Withdrawal** *(if applicable)*	• Complete withdrawal form on CRF if patient has ceased trial treatment or procedures but remains on follow up OR patient has withdrawn completely as did not provide consent and will not be followed up.	☐
13	**Non-compliance** *(if applicable)*	• Report any non-compliances on database and inform Warwick CTU ideally within 24 hours of becoming aware of the event	☐

RECOVERY-RS Trial Participant Completion Checklist V4.0 02.06.20

RECOVERY-RS
RESPIRATORY SUPPORT

Figure 1. RECOVERY-RS Trial Flowchart



RECOVERY-RS Trial Participant Completion Checklist V4.0 02.06.20

RECOVERY-RS
RESPIRATORY SUPPORT

Visit	1	2	3	4
Visit Window (No. Weeks ± No. Days)	**Day 0** Baseline	**Regular in-hospital reviews** (at least weekly)	**Day 30** (+/- 2 days)†	**Hospital discharge†**
Baseline data collection	✓			
Randomisation	✓			
Intervention	✓*	✓*		
Adverse events		✓	✓	✓
Survival status		✓	✓	✓
Outcome assessment			✓	✓

*- Intervention will be delivered up to point of death, tracheal intubation, or clinical determination that no ongoing need (palliation or improvement).
†- Participants to be followed-up to day 30 or hospital discharge, whichever comes later

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Tips for recruitment

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1. **Embed RECOVERY-RS in to patient care pathways** – consider for all suitable patients

2. **Develop a collaborative team** – engage respiratory, acute medicine, critical care, critical care outreach and AHP teams to capture patients at the right time

3. **Capture patients early on** – engage with the Emergency department and ward teams to identify potential participants patients early

4. **Avoid crossover** – provide training and clear communication between teams regarding allocated treatment arm. We still do not know the answer

5. **RECOVERY-RS remains an Urgent Public Health trial** – communicate to the Warwick CTU team or your local CRN if you need further support

Questions?

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