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A study to see whether the lungs of very sick patients on an artificial lung machine heal more quickly with slower, deeper breathing

Submission date
08/09/2025

Recruitment status
Not yet recruiting

Registration date
09/09/2025

Overall study status
Ongoing

Last Edited
03/12/2025

Condition category
Respiratory

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims

Acute Respiratory Distress Syndrome (ARDS) is a serious condition where the lungs become inflamed and injured, making it difficult for the body to get enough oxygen. This happens for many reasons, like infections (such as pneumonia), trauma, sepsis, or pancreatitis. ARDS can happen to anyone, no matter their age, and it's a major cause of death, with survival rates lower than 60%. For those who survive, the recovery can be long and tough, with lasting effects like difficulty exercising, mental health struggles, and a lower quality of life that can last for years. A study of intensive care units (ICUs) across 50 countries found that about 10% of ICU patients develop ARDS, and 23% of those who need a ventilator end up with the condition.

Ventilators can help save lives, but they can also cause more damage to the lungs (called ventilator-induced lung injury or VILI). To reduce this damage, doctors use techniques like lower air pressure or placing patients on their stomachs. Still, some ARDS patients continue to worsen despite these efforts and need extra support through a treatment called veno-venous extracorporeal membrane oxygenation (VV-ECMO). This involves a machine that takes over the oxygen exchange in the body, allowing doctors to reduce the need for the ventilator and further lung damage. Unfortunately, there are no specific drugs to treat ARDS yet, and the focus remains on supporting the patient and treating the cause of the condition.

The positive effects of using a lung protection strategy during ventilation and supporting patients with VV-ECMO (a machine that helps with oxygen exchange) in ARDS have been clearly shown to improve survival. Patients who need ECMO typically have the most severe form of ARDS and are still at risk for further lung damage, even when doctors try to reduce the intensity of the breaths they receive. Right now, doctors use a lung protection strategy that reduces the amount of air pushed into the lungs, keep the pressure low and try to keep the lungs open. This is considered the standard of care. But there's still a lot of uncertainty around the best way to ventilate ARDS patients who are also on ECMO, because no large, well-designed clinical trial has yet determined whether current strategies are fully protecting the lungs from damage. As the use of ECMO is growing worldwide, more research is urgently needed to figure out the best ventilation practices for these patients, with the goal of reducing the time they need ECMO, lowering the risks of complications, and improving survival rates.

For the most severely affected ARDS patients who require ECMO, the best way to minimize

ventilator-induced lung injury (VILI) is by reducing the frequency of breaths, as this is the main factor contributing to lung damage. This would allow the ECMO machine to handle the majority of the gas exchange. Some studies have looked into using complete apnoeic ventilation (where the ventilator doesn't breathe for the patient at all) to achieve this. However, the key issue is that the use of complete apnoea, means the lungs aren't being ventilated, and they can collapse, leading to atelectasis (lung tissue collapse). When ventilation is resumed, this can make it harder to re-expand the lungs and can even increase the risk of further injury due to high pressure or stress on the lung tissue. Additionally, when the lungs are inactive for too long, this can lead to poor lung compliance, meaning the lungs don't expand and contract as easily, which makes mechanical ventilation harder to manage.
Near apnoeic ventilation (NAV), offers a balanced approach: it keeps lungs almost at complete rest (minimizing ventilator-induced injury), but uses a few deeper breaths each minute (called sigh breaths) to maintain lung openness and reduce uneven stress across the lung and avoids lung collapse. This approach could help ARDS patients on ECMO recover faster, potentially reducing ECMO time, ventilator duration, and ICU stays—though more research is needed to confirm these real-world outcomes.
The aim of our study is to test if near apnoeic ventilation in ARDS patients on ECMO with just two sigh breaths per minute is better than what doctors use at the moment, which is varied between 10 and 30 breaths per minute. We hope that using only two deep sigh breaths will allow the lungs to recover quicker and patients will need less time receiving ECMO and mechanical ventilation reducing the risks of VILI.

Who can participate?
Patients aged 18 years and over in the ICU receiving invasive mechanical ventilation for severe ARDS being considered for ECMO

What does the study involve?
A participant in the study, will be randomly assigned to one of two groups by chance (like flipping a coin). They may not know which group they were allocated, but the study doctor and team will know. One group will receive two sigh breaths and the other normal standard ventilation while on ECMO. They will receive this ventilation method for the first three days on ECMO and then it will be up to the clinical team to decide on continuing with the two breaths or, if the lungs are recovering, to return to usual settings on the ventilator.
A participant will also be asked if they agree to blood and lung fluid samples being collected. These samples will allow us to investigate how the different types of ventilation affect the patient and better understand ARDS and how the ventilator damages the lungs more fully.
The doctors and nurses will also record ventilator and ECMO settings and patient observations, for example blood pressure, and document the medications and treatments they give the participant as part of their routine care. The research team will collect some of this data where relevant to this study.
Participants will be followed up by the clinical research team daily whilst in ICU. Once the participants have left the ECMO ICU and been discharged to the referring hospital, they will be followed up prior to hospital discharge from the referring hospital. Follow-up at 6 and 12 months will be via either electronic/postal/telephone questionnaires, medical records and data linkage with NHS Digital (eDRIS in Scotland) records wherever possible.

What are the possible benefits and risks of participating?
We cannot promise that the study will benefit the person participating in the study but the information we get from this study may help patients in the future. Their involvement in the study may help us understand and reduce the possible complications associated with mechanical ventilation whilst on ECMO support. Their biological samples and data could improve our understanding of 'restful' and 'moderate' support to a patient's breathing.

The risks of being on two breaths per minute from the ventilator is low as the function of the lungs is completely taken over by the ECMO machine. Risk is low from biological sampling – samples are taken alongside routine clinical blood samples using the same blood lines that have already been connected to the participant's body. Bronchoscopy is a standard procedure performed on ICU to obtain lung fluid samples

Where is the study run from?
Imperial College London (UK)

When is the study starting and how long is it expected to run for?
June 2024 to October 2029

Who is funding the study?
National Institute of Health Research Efficacy and Mechanism Evaluation (EME) Project: NIHR158537 (UK)

Who is the main contact?
1. Dr Sharon Mumby, romeo@imperial.ac.uk
2. Dr Brijesh Patel, romeo@imperial.ac.uk

Contact information

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Principal investigator

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Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
England 351190, Scotland 359602

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 60024, NIHR158537

Study information

Scientific Title
Rest Or Moderate mechanical ventilation during ECMO support

Acronym
ROMEO

Study objectives
Primary Objective:
To undertake a clinical efficacy study investigating near apnoeic ventilation (NAV) with two sigh breaths per minute after initiation of veno-venous Extracorporeal membrane oxygenation (VV-ECMO) for acute respiratory distress syndrome (ARDS), in comparison with standard ventilation with respiratory rate greater or equal to 10 breaths per minute.

Secondary Objectives:
Determine the impact of NAV on several short and long-term participant related outcome measures.

Tertiary Objectives:
Pathobiological and physiological mechanistic evaluation of differential treatment effect of near-apnoeic ventilation through analysis of biological samples (blood, bronchoalveolar lavage, and bronchial brushings) and analysis of granular physiological measurements.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 10/10/2025, London – Harrow REC (Health Research Authority, 2 Redman Place, Stratford, E20 1JQ, UK; +44 (0)207 1048 154; harrow.rec@hra.nhs.uk), ref: 25/LO/0660
2. Approved 04/11/2025, Scotland A REC (Manx Neill, Scotland A & B REC Manager; +44 (0) 7814609032; manx.neill@nhslothian.scot.nhs.uk), ref: 25/SS/0077

Study design
Randomized; Interventional; Design type: Process of Care, Device

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Acute respiratory distress syndrome (ARDS)

Interventions
This study is a two-arm, parallel-group, multi-centre, open-label, individually randomised controlled trial of rest or moderate mechanical ventilation in patients under ECMO support, with a 6-month internal pilot to monitor screening and recruitment.

The trial will be performed at 9 ECMO sites in the UK. We hope to enrol 364 participants (182 per group). Eligible participants will be randomised to one of two ventilation strategies – near apnoeic ventilation with two sigh breaths vs standard ultraprotective ventilation (10 or more breaths per minute).

Patients will only be considered eligible if they are over 18 years and have been diagnosed with ARDS and require VV-ECMO.

In addition, patients are not considered eligible due to being aged under 18, >48 hours from VV-ECMO initiation, consent declined, treatment withdrawal imminent within 48 hours, or the presence of bronchopleural fistula.

For each patient, if identified as eligible, advice to participate in the study will be sought. Critically ill patients are and often unconscious and may not be able to grant consent. Therefore, the Patient Informed Sheet (PIS) and Declaration Form will be requested from a third party acting as a representative; in most cases this person will be a Personal Legal Representative, (in Scotland This person will be the participant's Welfare Attorney/Welfare Guardian/Nearest Relative) who is someone who knows the person lacking capacity and is able to advise the researcher about that person's wishes and feelings in relation to the project and whether they should join the research. This person must be interested in the welfare of the patient in a personal capacity, not in a professional capacity or for remuneration and will mostly likely be a family member, carer or friend, etc.

Where the PerLR (or in Scotland the Welfare Attorney/Welfare Guardian/Nearest Relative) is not available on site, the researcher may contact them by telephone/online and seek verbal advice. The verbal agreement will be recorded in the Remote PerLR declaration (or in Scotland the remote Welfare Attorney/Welfare Guardian/Nearest Relative form). The Remote PerLR (or in Scotland the remote Welfare Attorney/Welfare Guardian/Nearest Relative) declaration form will be signed by a second member of staff who has witnessed the telephone/online advice. A copy of the PIS will be emailed to the PerLR (or in Scotland the Welfare Attorney/Welfare Guardian /Nearest Relative).

In England only, where no PerLR is available, the researcher will nominate a professional person to assist in determining the participation of a person who lacks capacity. A Professional Legal

Representative (ProLR) is someone who will be appointed by the researcher to advise the researcher about the person's (who lacks capacity) wishes and feelings in relation to the project and whether they should join the research. An independent clinician not treating the patient will be asked to be the ProLR. A patient information sheet will be distributed immediately following the patient being identified as eligible for the study.

Those deemed eligible and who provide consent through a legal representative (or in Scotland a Welfare Attorney/Welfare Guardian/Nearest Relative) will be randomly assigned to receive either conventional mechanical ventilation or near-apnoeic ventilation (NAV). The randomisation process will be conducted through a web-based system, utilising a stratified permuted block design. Stratification will be based on the site of recruitment and the duration of invasive mechanical ventilation pre-ECMO (≤72 h vs >72 h).

Intervention Type
Other

Primary outcome(s)
The time from randomisation to successful decannulation from VV-ECMO (defined as 48 hours free of ECMO), incorporating death as a competing risk

Key secondary outcome(s))
Secondary outcomes represent the core outcomes defined for trials of mechanical ventilation and ECMO. These include:
1. Days alive and free of ECMO (DAFE) up to day 28 and 60
2. Daily Organ Support for participants on ECMO (DOSE) score up to 28 days post-randomization
3. Mortality recorded at 60 days, 6 months, and 1 year
4. First successful liberation from invasive mechanical ventilation, i.e. >48 hours of spontaneous ventilation (CPAP or HFNC)
5. Duration of invasive mechanical ventilation
6. Serious adverse events recorded to hospital discharge (including AEs of specific interest related to NAV and ECMO as listed below)
7. Length of total ICU and hospital stay
8. Health-related quality of life measured using EQ-5D-5L at 6 and 12 months
9. Disability measured using the Modified Rankin Scale at 6 and 12 months

Completion date
31/10/2029

Eligibility

Key inclusion criteria
1. Reversible cause of ARDS as determined by the treating physician prior to VV-ECMO cannulation
2. Adult participants (18 years and over) undergoing invasive mechanical ventilation
3. Requiring VV-ECMO for severe ARDS. Within the context of this study, 'ARDS' will be defined using the Berlin definition criteria applied prior to ECMO cannulation:
3.1. Symptoms must appear within one week of a known clinical event or worsen within that time
3.2. Chest x-ray or CT scan must show bilateral opacities that aren't fully explained by other factors
3.3. Respiratory failure can't be caused by cardiac failure or fluid overload
3.4. The ratio of partial pressure of oxygen in arterial blood (PaO2) to the fraction of inspired

oxygen (FiO2) determines the severity of ARDS:
3.4.1. Mild ARDS: PaO2/FiO2 of 200-300 mmHg / 27-40 kPa
3.4.2. Moderate ARDS: PaO2/FiO2 of 100-200 mmHg / 13-27 kPa
3.4.3. Severe ARDS: PaO2/FiO2 less than 100 mmHg / 13 kPa

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
99 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. >48 hours from VV-ECMO initiation
2. Participant likely to die or withdrawal of life sustaining therapy within 48 hours
3. Bronchopleural fistula

Date of first enrolment
05/01/2026

Date of final enrolment
31/10/2028

Locations

Countries of recruitment
United Kingdom

England

Scotland

Study participating centre
Guy's and St Thomas' NHS Foundation Trust
St Thomas' Hospital

Westminster Bridge Road
London
England
SE1 7EH

Study participating centre
Royal Papworth Hospital NHS Foundation Trust
Papworth Road
Cambridge Biomedical Campus
Cambridge
England
CB2 0AY

Study participating centre
King's College Hospital NHS Foundation Trust
Denmark Hill
London
England
SE5 9RS

Study participating centre
Grampian
Summerfield House
2 Eday Road
Aberdeen
Scotland
AB15 6RE

Study participating centre
University Hospitals of Leicester NHS Trust
Leicester Royal Infirmary
Infirmary Square
Leicester
England
LE1 5WW

Study participating centre
Manchester University NHS Foundation Trust
Cobbett House
Oxford Road
Manchester

England
M13 9WL

Study participating centre
University Hospitals Bristol and Weston NHS Foundation Trust
Trust Headquarters
Marlborough Street
Bristol
England
BS1 3NU

Study participating centre
Barts Health NHS Trust
The Royal London Hospital
80 Newark Street
London
England
E1 2ES

Study participating centre
Guy's and St Thomas' NHS Foundation Trust
Royal Brompton Hospital, Sydney Street
London
England
SW3 6NP

Sponsor information

Organisation
Imperial College London

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes