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Airway Pressure Release Ventilation (APRV) vs conventional ventilation for patients with moderate to severe acute hypoxemic respiratory failure:
The RELEASE Trial

Welfare Attorney/Welfare Guardian or Nearest Relative Information Leaflet

Invitation to take part in a research study

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- This information sheet explains the RELEASE trial and what taking part will involve
- The RELEASE trial is looking to see if Airway Pressure Release Ventilation (APRV) which is a way of using the breathing machine helps patients with diseased lungs to heal faster and spend less time on a ventilator compared to the usual way breathing support is given in critical care.
- We are approaching you because the person you are consenting for is unable to decide for themself whether to participate in this research. To help decide if they should join the study, we would like to ask your opinion whether or not they would want to be involved.
- It is important that you put aside your own feelings and wishes and consider what the past and present, feelings and wishes of the person you are consenting for would have been, had they been able to consent for themselves.
- APRV is used as part of routine care in some UK critical care units (CCU), so we do not anticipate any serious risk to the person you are consenting for by taking part.
- If you decide that the person you are consenting for would like to take part, we will ask you to read and sign the consent form.

- We will collect identifiable data from medical records and national datasets from the person you are consenting for and ask them to complete questionnaires at 2 and 6 months after leaving hospital to see how they are getting on.
- We will keep you fully informed during the study so you can let us know if you have any concerns.
- If you are unsure about taking on the role of Welfare Attorney/Welfare Guardian or Nearest Relative, you may seek independent advice. We will understand if you do not want to take on this responsibility.
- If you decide that the person you are consenting for would not wish to take part to this study, it will not affect the standard of care in any way.
- When the person you are consenting for is better, we will provide them with the same information and ask them for consent to carry on in the study. They will have the opportunity to make decisions about the use of the information we have collected about them up until that point.
- The University of Warwick is currently leading several studies looking at how we treat patients with respiratory failure. The person you are consenting for may already be in one of those studies. If so, we may share information between these studies to reduce what we need to ask from the person you are consenting for.

Before you decide, please read the information carefully to understand why the research is being done. Talk to others about the study if you wish and please feel free to ask us any questions.

Our animated trial summary video can be accessed by scanning the below QR code or via: www.explainmytrial.com/release

There is separate data information which describes how we will use data collected about the person you are consenting for and can be accessed on the study website https://warwick.ac.uk/release-trial/public/, via the QR code at the end of this leaflet or a member of staff can print a copy for you.

Why are we doing this study?

Around half of all patients in critical care need help from a breathing machine (ventilator) to maintain oxygen levels. Although they may be life-saving, breathing machines can cause damage to diseased lungs and make chest infections more likely.

The usual way a breathing machine is used aims to protect lungs from damage until they are healed. However, damage can still occur, and lungs take time to recover. Airway Pressure Release Ventilation (APRV) is a way of using the breathing machine that we think causes less damage. It moves gas into the lungs gently over a longer time. This helps to reduce lung damage, helping faster healing. APRV may reduce time on the breathing machine and in hospital which may save costs. APRV may also reduce the risk of death.

We are doing this study to find out if setting the breathing machine to deliver breaths using APRV helps patients with diseased lungs to heal faster and spend less time on a ventilator compared to the usual way breathing support is given in critical care. We also want to know if APRV saves more lives, improves quality of life, and saves the NHS money by helping people leave CCU sooner.

Why are you being approached on behalf of the person you are consenting for?

We are asking you about the person you are consenting for because they are in critical care, and it is not possible to ask them about their views about taking part in this study. We would like you to consider their views and interests on whether they would want to be involved based on what you know of their wishes and feelings. Please let us know of any advance decisions the person you are consenting for may have made about them participating in research studies.

If you think they would like to take part, we will ask you to sign a consent form. We will give you a copy of the form to keep. When the person you are consenting for becomes well enough, we will give them the information about the trial and discuss their participation with them. They will have the opportunity to make decisions about the use of the information we have collected about them up until that point. In total we will be including 710 patients from across the UK in this study.

Who is eligible for the study?

Patients admitted to a CCU in the UK who are:

- Aged 18 years or more
- Receiving support from a breathing machine
- Have moderate to severely low oxygen levels
- Are expected by the critical care team to stay on a breathing machine for more than two days

Does the person you are consenting for have to take part?

No, taking part in this study is completely voluntary. Even if you agree for the person you are consenting for to be in the study, you can change your mind and withdraw them at any time without

giving a reason, but we will keep the data we already have collected and we will ask permission to continue to collect some data. They will receive the same standard of care, and this decision will have no influence on their further treatment.

What does this study involve?

The person you are consenting for will be assigned by chance (randomised) to one of two groups.

1. APRV: The breathing machine will be set to the APRV mode. APRV moves gas into the lungs gently over a longer time. APRV is available on all ventilators that are used within the NHS.
2. Usual care: The breathing machine will be set as usual by the critical care team.

There will be no other changes to care delivered by the critical care team for patients in both the APRV and usual care group.

You, the research team, or the critical care team will not be able to choose which group the person you are consenting for is in. This is decided by a computer at random, just like tossing a coin or drawing lots.

The research team will collect information about the care the person you are consenting for receives while in critical care including how the breathing machine is used, how long they need the machine, and how long they stay in critical care. The research team will collect personal information from the person you are consenting for such as age, ethnicity, sex and past medical conditions before coming to critical care as this helps us to understand the effect of APRV on different groups of people.

After leaving the hospital, the person you are consenting for will be sent a questionnaire two and six months after hospital discharge asking about their overall wellbeing and quality of life. Each questionnaire will take approximately five to ten minutes to complete. Questionnaires will be sent via text, email or post, or answers collected via the telephone. If needed, someone can complete them on behalf of the person you are consenting for. We may share the name, email address, and phone number of the person you are consenting for with a third-party company in order to send them the questionnaires by text message or email. We may also get in touch with the person you are consenting for by text message, email or telephone if we have any queries about their questionnaire or if we have any updates related to the study.

How long does the study last?

The person you are consenting for will remain in the study for six months after hospital discharge to complete the questionnaire about their overall wellbeing and quality of life.

Optional blood and urine sampling

All patients participating in the trial have the opportunity to provide blood and urine samples for future research. Samples will be taken on three days whilst the person you are consenting for is

ventilated. The amount of blood taken on these days for research is small (20 ml each time or approximately 4 teaspoons). 5ml of urine would also have been taken on these days.

Blood and urine samples will be sent and stored at Queen's University Belfast. Storage of these samples will enable us to undertake more research if new knowledge or technology becomes available. We do not know for sure what these future studies will be, but they may involve genetic analysis, sharing samples with collaborators abroad or research in collaboration with partners such as commercial companies. If this happens, the samples shared would be anonymous and external investigators or organisations would not be able to identify the person you are consenting for.

Anonymised data collected as part of the study may also be used to understand the sample analyses. You can indicate on the consent form if you agree to let us retain samples for future use. All projects involving their blood and urine will be reviewed by an external committee of experts, which will safeguard the ethical use of them.

You can change your mind any time in the future and request for samples from the person you are consenting for to be destroyed without giving any reason by contacting the hospital research team. However, if they have already been used for research, it will not be possible to withdraw any data or findings from work completed using these samples.

What are the benefits of taking part?

As this is a research study, the person you are consenting for may or may not experience a direct benefit. However, the findings of the study may help people needing a breathing machine in critical care in the future.

There is no payment for taking part in this study. However, to thank the person you are consenting for for their time in completing the follow-up questionnaires at two-months and six-months, we will provide a small monetary gift voucher.

The University of Warwick is currently leading several studies looking at how we treat patients with respiratory failure. This group of studies is called the 'Confederation of Respiratory Critical Care Trials' or 'CoReCCT'. If the person you are consenting for are taking part in other studies within CoReCCT, they will not need to complete questionnaires for each study. They will only be asked to complete the questionnaires once and will receive one voucher with each questionnaire.

What are the risks of taking part?

APRV is used as part of routine care in some CCUs for patients with very sick lungs. Therefore, we do not anticipate any serious risk to the person you are consenting for specific to being in the APRV group. However, all patients who are very sick and need a breathing machine are at risk of complications such as damage to the lungs or needing the breathing tube put back in after it is removed due to ongoing problems with breathing. Some very sick patients may even die.

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What if new information becomes available?

Sometimes during a research study, new information becomes available about the study treatment(s). If this information changes the involvement of the person you are consenting for in the study, the study treatment may be stopped and they will continue to receive the usual standard of care.

How will we keep their data confidential?

In this research trial we will use information from the person you are consenting for, their GP, their medical records, and healthcare databases such as NHS England. We will only use information that we need for the trial.

Everyone involved in this trial will keep their data safe and secure. We will also follow all privacy rules. At the end of the trial we will save some of the data in case we need to check it and for future research. We will make sure no-one can work out who the person you are consenting for is from the reports we write.

For details on how data is used and kept safe, visit https://warwick.ac.uk/release-trial/public or scan the QR code at the end of this leaflet. If you prefer a printed copy please ask a member of staff.

What if there is a problem?

If you have any concern about any element of this trial, you can contact the researchers at your hospital: **[insert PI contact details]**

You can also seek advice from: **[insert relevant local contact]**

If you remain unhappy and wish to complain formally, you can do this by contacting the person below, who is a senior University of Warwick official and is independent of this study:

Head of Research
Governance Research & Impact Services
University House
University of Warwick
Coventry
CV4 8UW
Tel: 02476 575733
Email: researchgovernance@warwick.ac.uk

The University of Warwick will provide indemnity for this trial. If you are harmed due to someone's negligence, you may have grounds for legal action which you may have to pay for. NHS bodies may also be liable if you are harmed as a result of negligence whilst taking part in a clinical trial. Non-

negligent harm by NHS staff is not covered by the NHS indemnity scheme, and therefore compensation may not be paid in these circumstances.

Who is organising and paying for the study?

This study is sponsored by Warwick University and is being coordinated by the Warwick Clinical Trials Unit. The study is funded by the National Institute for Health Research, Health Technology Assessment (NIHR154501). The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

Who has reviewed this study?

People with personal experience of having respiratory failure and other members of the public have helped design and set up this study.

Research in the NHS that involves patients is reviewed by an independent group of people called a Research Ethics Committee (REC). This committee is there to protect your interests. This study has been reviewed and been approved by Scotland A REC.

Contact for further information:

If you have any questions about the study, either now or in the future, you may contact your local research team at <<local research contact details>>

You may also wish to seek the advice of an independent contact who has knowledge of the study but is not directly involved with the study

<<independent contact details>>

Alternatively, please contact the RELEASE trial manager at Warwick University:
Email: RELEASE@warwick.ac.uk

An online version both this information leaflet and the data information leaflet can be found on the study website, or by scanning the QR code below:
https://warwick.ac.uk/release-trial/public/

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Thank you for taking the time to read this information and for considering if the person you are consenting for should take part in this study.

Funded by NIHR | National Institute for Health and Care Research