ISRCTN13384956 https://doi.org/10.1186/ISRCTN13384956

Intensive care unit randomised trial comparing two approaches to oxygen therapy (UK-ROX)

Submission date
08/12/2020

Recruitment status
No longer recruiting

Registration date
08/12/2020

Overall study status
Completed

Last Edited
16/06/2025

Condition category
Other

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Each year, around 184,000 patients are admitted to NHS intensive care units (ICUs) and over 30% require help with their breathing using a ventilator (breathing machine). Giving oxygen through the ventilator is an essential part of this treatment. However, currently it is not known how much oxygen should be given to patients to optimise their recovery. Both too much and too little oxygen may cause harm. The concentration of oxygen given through the ventilator is adjusted according to how much oxygen can be detected in a patient's blood, known as 'oxygen saturation'. Some studies have shown that in unwell hospitalised patients, having a lower, rather than higher, oxygen saturation may more be beneficial. The aim of this study is to find out whether using a lower oxygen target (conservative oxygen therapy) to guide oxygen treatment might lead to better outcomes for patients when compared with the approach currently used in NHS ICUs (usual oxygen therapy).

Who can participate?
Patients aged 18 and over receiving invasive mechanical ventilation and supplemental oxygen from about 100 UK NHS ICUs

What does the study involve?
Eligible patients will be randomly allocated to either the conservative oxygen therapy or the usual oxygen therapy group. If a patient is allocated to conservative oxygen therapy (intervention) group, the lowest concentration of oxygen possible should be administered to maintain the patient's oxygen at 90 (±2)%. For patients receiving oxygen, it should not rise above 92%. Alarms should be set to prevent an SpO_2 lower than 88% and higher than 92%. If a patient is allocated to the usual oxygen therapy (control) group, the clinical team will continue to deliver oxygen therapy as per local practice and clinical management will not be influenced by the trial. The researchers will follow all patients up to 90 days later by 'linking' study data with routinely collected national records. They will also send a questionnaire to around 15% of surviving patients at 90 days to find out about their quality of life and use of health services. They will find out if conservative oxygen therapy was more effective than usual oxygen therapy by comparing the number of patients alive in each group at 90 days.

What are the possible benefits and risks of participating?
Extremely high and extremely low oxygen levels can cause damage to the body. The purpose of this study is to look at the effect of a small reduction in oxygen given. The benefits and risks of giving slightly less oxygen are unclear at this time, which is why this research is needed.

Where is the study run from?
Intensive Care National Audit & Research Centre (ICNARC) (UK)

When is the study starting and how long is it expected to run for?
August 2020 to August 2025

Who is funding the study?
National Institute for Health Research (NIHR) – Health Technology Assessment (HTA) Programme (UK)

Who is the main contact?
Ms Tasnin Shahid
UK-ROX@icnarc.org

Study website
https://www.icnarc.org/Our-Research/Studies/Uk-Rox

Contact information

Type(s)
Public

Contact name
Ms Tasnin Shahid

ORCID ID
https://orcid.org/0000-0003-4320-6140

Contact details
Intensive Care National Audit & Research Centre (ICNARC)
Napier House
24 High Holborn
London
United Kingdom
WC1V 6AZ
+44 (0)20 7269 9277
tasnin.shahid@icnarc.org

Type(s)
Scientific

Contact name
Prof Daniel Martin

ORCID ID
https://orcid.org/0000-0001-6220-8235

Contact details
Peninsula Medical School
University of Plymouth
John Bull Building
Derriford
Plymouth
United Kingdom
PL6 8BU
+44 (0)2072699277
daniel.martin@plymouth.ac.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
288506

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 46926, IRAS 288506, HTA - NIHR130508

Study information

Scientific Title
Evaluating the clinical and cost-effectiveness of a conservative approach to oxygen therapy for invasively ventilated adults in intensive care

Acronym
UK-ROX

Study objectives
In non-elective adults receiving mechanical ventilation and supplemental oxygen in the intensive care unit, conservative oxygen therapy is superior to usual oxygen therapy, in terms of all-cause mortality at 90 days.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 17/02/2021, South Central – Oxford C Research Ethics Committee (South Central – Oxford C Research Ethics Committee Level 3, Block B, Whitefriars Building, Bristol Research Ethics Committee Centre, BS1 2NT, UK; +44 (0)207 104 8226; oxfordc.rec@hra.nhs.uk), REC ref: 20/SC/0423

Study design

Randomized; Interventional; Design type: Treatment, Process of Care, Management of Care

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
The participant information sheets will be made publicly available on the ICNARC website once REC approval is received (https://www.icnarc.org/Our-Research/Studies/Uk-Rox)

Health condition(s) or problem(s) studied
Invasive ventilation in intensive care

Interventions
Current interventions as of 20/04/2021:
Patients will be randomly allocated ("randomized"), in a 1:1 ratio, to one of two treatment groups: conservative oxygen therapy (intervention) or usual oxygen therapy (control). Each participant will have a 50/50 chance of being enrolled in the intervention or control group. Patients receiving supplemental oxygen during invasive mechanical ventilation in ICUs will eligible for the trial. The trial interventions are intended to be delivered early in the course of mechanical ventilation, just as would be the case in standard NHS practice, and therefore patients must be randomised within 12 hours of meeting the eligibility criteria.

If a patient is randomized to the usual oxygen therapy (control) group, the clinical team will continue to deliver oxygen therapy as per local practice and clinical management will not be influenced by the trial. The intervention should be continued until discharge from ICU, or 90 days after randomisation, whichever is sooner. If a participant is readmitted to ICU within the 90 days, the intervention should be recommenced.

If a patient is randomized to conservative oxygen therapy (intervention) group, the lowest concentration of oxygen possible should be administered to maintain the patient's oxygen at 90 (±2)%. For patients receiving oxygen, it should not rise above 92%. Alarms should be set to prevent an SpO_2 lower than 88% and higher than 92%. The intervention remains the same once a patient is extubated, regardless of the modality by which they receive oxygen therapy. The intervention should be continued until discharge from ICU, or 90 days after randomisation, whichever is sooner. If a participant is readmitted to ICU within the 90 days, the intervention should be recommenced.

In both groups, all other treatments and procedures will be carried out in accordance with standard NHS care and local practice. As eligible patients will be critically ill and on an invasive mechanical ventilator at the point in which they become eligible for UK-ROX – a model of

research without prior consent (RWPC) (also known as 'deferred consent') will be used. At 90 days, 15% of participants will be posted a questionnaire about health-related quality of life and their use of health services since leaving hospital.

Previous interventions:
Patients will be randomly allocated ("randomized"), in a 1:1 ratio, to one of two treatment groups: conservative oxygen therapy (intervention) or usual oxygen therapy (control). Each participant will have a 50/50 chance of being enrolled in the intervention or control group. Patients receiving supplemental oxygen during invasive mechanical ventilation in ICUs will eligible for the trial. The trial interventions are intended to be delivered early in the course of mechanical ventilation, just as would be the case in standard NHS practice, and therefore patients must be randomised within 12 hours of meeting the eligibility criteria.

If a patient is randomized to the usual oxygen therapy (control) group, the clinical team will continue to deliver oxygen therapy as per local practice and clinical management will not be influenced by the trial. The intervention should be continued until discharge from ICU, or 90 days after randomisation, whichever is sooner. If a participant is readmitted to ICU within the 90 days, the intervention should be recommenced.

If a patient is randomized to conservative oxygen therapy (intervention) group, the clinical team will use an SpO_2 target range of 90-93%. the lowest concentration of oxygen possible should be administered to maintain the patient's SpO_2 at or just above 90%. For patients receiving oxygen, SpO_2 should not rise above 93%. Alarms should be set to sound at an SpO_2 of 89% and below and 94% and above. The intervention remains the same once a patient is extubated, regardless of the modality by which they receive oxygen therapy. The intervention should be continued until discharge
from ICU, or 90 days after randomisation, whichever is sooner. If a participant is readmitted to ICU within the 90 days, the intervention should be recommenced.

In both groups, all other treatments and procedures will be carried out in accordance with standard NHS care and local practice. As eligible patients will be critically ill and on an invasive mechanical ventilator at the point in which they become eligible for UK-ROX – a model of research without prior consent (RWPC) (also known as 'deferred consent') will be used. At 90 days, 15% of participants will be posted a questionnaire about health-related quality of life and their use of health services since leaving hospital.

Intervention Type
Procedure/Surgery

Primary outcome measure
Primary clinical outcome:
90-day all-cause mortality, assessed through review of patient medical notes at 90 days post-randomisation and/or data linkage with nationally held death registrations

Primary economic outcome:
Incremental costs, QALYs and net monetary benefit at 90 days, assessed by combining Health-related Quality of Life (EuroQol EQ-5D-5L questionnaire) data with valued resource use data obtained via a health services questionnaire and data obtained through linkage with national hospital episode statistics, death registrations and the national clinical audit for adult critical care.

Secondary outcome measures

1. ICU and hospital mortality (censored at 90 days), assessed through review of patient medical notes at the relevant timepoints and/or data linkage with nationally held death registrations
2. Mortality at 60 days and 1 year, assessed through review of patient medical notes at the relevant timepoints and/or data linkage with nationally held death registrations
3. Duration of ICU and acute hospital stay (censored at 90 days), assessed through data linkage with the national clinical audit for adult critical care
4. Days alive and free from organ support at 30 days (an ordinal outcome with death as the worst outcome). Defined as receipt of respiratory, cardiovascular or renal support within critical care according to the Critical Care Minimum Dataset (added 30/10/2024)
5. Health-related quality of life at 90 days, assessed using the EuroQol EQ-5D-5L questionnaire administered to patients at 90 days
6. Resource use and costs at 90 days, assessed by valuing resource use data obtained via a health services questionnaire administered to patients at 90 days and data linkage with national hospital episode statistics and the national clinical audit for adult critical care
7. Estimated lifetime incremental cost-effectiveness, estimated by combining 90-day HrQoL data with valued resource use data obtained via a health services questionnaire at 90 days, data obtained through linkage with national hospital episode statistics, death registrations and the national clinical audit for adult critical care

Overall study start date
01/08/2020

Completion date
01/08/2025

Eligibility

Key inclusion criteria
1. Aged ≥18 years
2. Receiving invasive mechanical ventilation in the ICU following an unplanned ICU admission (i.e. not admitted after an elective procedure) OR invasive mechanical ventilation started in the ICU (i.e. the patient was intubated in the ICU)
3. Receiving supplemental oxygen (fractional inspired concentration of oxygen (FiO_2) >0.21) at the time of enrolment

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 16,500; UK Sample Size: 16,500

Total final enrolment
16500

Key exclusion criteria
1. Previously randomised into UK-ROX in the last 90 days
2. The clinician considers that one study treatment arm is either indicated or contraindicated.

Removed 20/04/2021:
A data dictionary will contain relevant examples of conditions where clinicians may exclude patients (at their discretion) because conservative oxygen therapy is either indicated or contraindicated (e.g. chronic lung diseases, receiving hyperbaric oxygen, prior bleomycin exposure, carbon monoxide poisoning).

Added 22/02/2021:
3. Currently receiving extracorporeal membrane oxygenation (ECMO)

Date of first enrolment
03/05/2021

Date of final enrolment
27/11/2024

Locations

Countries of recruitment
United Kingdom

Study participating centre
Site identification is in progress
United Kingdom
-

Sponsor information

Organisation
Intensive Care National Audit & Research Centre (ICNARC)

Sponsor details
Napier House
24 High Holborn
London
United Kingdom
WC1V 6AZ
+44 (0)20 7269 9277
ctu@icnarc.org

Sponsor type
Research organisation

Website
http://www.icnarc.org/

ROR
https://ror.org/057b2ek35

Funder(s)

Funder type
Government

Funder Name
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC); Grant Codes: NIHR130508

Results and Publications

Publication and dissemination plan
1. The protocol will be made publicly available on the ICNARC and the NIHR websites, once REC approval is received (https://www.icnarc.org/Our-Research/Studies/Uk-Rox)
2. The protocol and statistical analysis plan will be submitted for publication prior to the end of the patient recruitment period.
3. The primary results of the trial will be submitted for publication in a high-impact peer-reviewed journal within 1 year of the overall trial end date

Intention to publish date
30/06/2025

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from the ICNARC CTU (UK-ROX@icnarc.org). Non-patient identifiable data, for participants who consented to data sharing, will be made available one year after the publication of the main trial results. Application requests will be reviewed and approved by the Chief Investigator(s) and the ICNARC CTU.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Protocol article		11/04/2024	08/07/2024	Yes	No
Results article		12/06/2025	16/06/2025	Yes	No