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Comparing standard and accelerated weaning from non-invasive breathing support in exacerbation of chronic obstructive pulmonary disease

Submission date 24/08/2022	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol
Registration date 14/09/2022	**Overall study status** Completed	[X] Statistical analysis plan [_] Results
Last Edited 07/05/2025	**Condition category** Respiratory	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims

Every year in the UK, over 141,000 people will be admitted to hospital due to exacerbations of chronic obstructive pulmonary disease (ECOPD). Around one-quarter of these patients develop life-threatening respiratory failure, with a build-up of carbon dioxide (waste gas). Non-invasive ventilation (NIV) involves wearing a tightly-fitted mask connected to a ventilator to help patients breathe out more carbon dioxide.

NIV halves the risk of dying but can cause unpleasant side effects including stomach bloating and skin damage. Once the patient is improving, NIV is gradually removed by giving patients progressively longer periods of time off ventilation. This is called ‘weaning’ and usually takes 3-4 days. Faster weaning should reduce side effects and costs. However shorter treatment may be less effective, and respiratory failure (carbon dioxide build-up) may recur. Currently, there is little evidence to guide a safe process for NIV weaning, with concerns highlighted in a National Confidential Enquiry.

Researchers have recently developed the NIV outcomes score, which predicts the risk of death in NIV-treated patients. They showed that three in four patients have a low or medium risk, and therefore it may be possible to remove the ventilator from this group of patients more quickly. They also noticed big differences between hospitals with respect to duration of weaning and patient relapse rates, highlighting the need for better guidance. They have developed an "accelerated weaning protocol" to support faster weaning from NIV, whilst also ensuring that the approach is consistent within the trial across all hospitals. This will be compared to the current standard approach.

The main question is whether "accelerated weaning" reduces the time required to successfully wean from NIV. If NIV is restarted within 48 hours of removal, this will be considered an unsuccessful weaning attempt and will be included in the time to weaning. Patient outcomes, including any increased risk of death, will be carefully monitored. The researchers will also assess the side effects from NIV, relapse, sleep quality, symptoms, quality of life, readmission into hospital, and costs.

Who can participate?
Patients aged 35 years and over, who are in hospital with ECOPD requiring NIV and have a low or medium risk NIV outcomes score will be considered for participation in the study. To ensure the results apply as widely as possible, patients with a clinical diagnosis of COPD, but without breathing tests to confirm this, will be included, and patients will only be excluded when essential.

What does the study involve?
Those who agree to take part will be randomly allocated by computer to a 'standard' or 'accelerated' weaning protocol. The standard wean involves increasing the amount of time off NIV over 3-4 days, with a final night on NIV after a full day off NIV. The accelerated wean involves a daily 4-hour trial without NIV under close monitoring. If the carbon dioxide levels in the blood are stable and safe, NIV will be stopped early.

What are the possible benefits and risks of participating?
As things stand, it is not known what the best amount of time is to be on NIV, and practice varies around the country. The researchers cannot guarantee any direct benefits, but by taking part, participants will be helping healthcare professionals about how best to treat their patients in the future, which may include the participants.
The researchers will ask participants some extra questions about how they are feeling, which will take up a short amount of their time both in hospital and after they have gone home. They will try and keep this amount of time to a minimum.
Whichever group patients are randomly assigned to there is a risk of needing the ventilator for longer than anticipated, or extra blood tests. The researchers will always try and keep extra tests to a minimum, patient safety is the priority.

Where is the study run from?
The study is being led by Northumbria Healthcare NHS Foundation Trust, but to ensure the results apply across the NHS, we will include several hospitals across England (UK)

When is the study starting and how long is it expected to run for?
April 2022 to June 2025

Who is funding the study?
National Institute for Health Research, Research for Patient Benefit (UK)

Who is the main contact?
Prof. Stephen Bourke, Stephen.Bourke@northumbria-healthcare.nhs.uk

Contact information

Type(s)
Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
313485

ClinicalTrials.gov number

Nil known

Secondary identifying numbers
CPMS 53277, IRAS 313485, Protocol v1.1 (05/08/2022)

Study information

Scientific Title
Standard versus accelerated weaning from non-invasive ventilation (NIV) in chronic obstructive pulmonary disease directed by the NIV outcomes score: a randomised controlled trial

Acronym
NIVOW

Study objectives
Daily 4-hour unsupported breathing trials, with the removal of non-invasive ventilation (NIV) if the patient remains clinically and physiologically stable, will shorten the time to successful wean from NIV, compared to the standard protocol in exacerbations of chronic obstructive pulmonary disease (ECOPD) with a low or medium mortality risk.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 08/09/2022, West of Scotland Research Ethics Service (Ward 11, Dykebar Hospital, Grahamston Road, Paisley, PA2 7DE, UK, +44 (0)141 314 0212; WosRed@ggc.scot.nhs.uk), ref: 22/WS/0091

Study design
Multi-centre open-label parallel randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Exacerbation of chronic obstructive pulmonary disease (COPD)

Interventions
Patients with exacerbation of COPD requiring NIV who have low or medium risk NIV outcomes scores will be assessed against the full selection criteria detailed below. Consenting patients who meet the eligibility criteria will be independently randomised on a 1:1 basis between the two treatment strategies, performed independently (sealedenvelope.com) using minimisation to ensure groups are balanced for: a) NIV Outcomes score: low or medium risk; b) Site; c) HCO_3-: <28 or ≥28; d) pH: <7.18 or ≥7.18; e) previous NIV: yes or no.

Standard weaning protocol: Progressively longer periods off NIV, determined by arterial blood gas (or capillary blood gas), with a final night on NIV after a full day off NIV.

Accelerated weaning protocol: Daily 4-hour weaning trial, success confirmed by arterial blood gas, with additional transcutaneous carbon dioxide monitoring.

The weaning time endpoint is the date and time that the NIV mask is removed from the patient's face for the final time (provided NIV does not need to be recommenced within 48 hours).

Intervention Type
Procedure/Surgery

Primary outcome measure
Time to successful weaning: duration from the baseline arterial blood gas confirming selection criteria met, to final removal of the ventilator. Death on NIV precludes weaning and will be captured in a competing risk analysis.

Secondary outcome measures
1. Relapse requiring NIV (defined as recurrent acute hypercapnic respiratory failure (AHRF) >48 hours after removal of the ventilator)
2. Total duration of ventilation measured from the time the NIV mask is applied to NIV mask removal
3. Length of hospital stay from arrival to discharge measured using medical records/hospital patient administration system
4. NIV complications (incidence and severity) in hospital, measured by daily recording
5. Patient-reported outcome measures at days 7, 30 and 90 post-randomisation:
5.1. How breathless the patient feels, measured using the Modified Borg dyspnoea scale
5.2. Sputum clearance measured using a visual analogue scale
5.3. How well or poorly the patient feels they have slept the previous night, measured using the Richards-Campbell sleep questionnaire (all measured days 1 to 5 from the start of weaning)
5.4. Patient's mood for anxiety and depression measured using the Hospital Anxiety and Depression Scale (HADS) pre-discharge
5.5. Quality of life related to COPD measured using the St Georges Respiratory Questionnaire for COPD (SGRQ-C)
5.6. Quality of life measured using EQ-5D-5L
6. Mortality in-hospital and 90-days post-randomisation measured using medical and GP records /electronic patient administration system
7. Readmissions 30-days post-discharge measured using patient self-completed health resource use diary and verified with hospital electronic patient administration system and primary care records
8. Health economic analysis:
8.1. Costs to the NHS in terms of provision of the interventions (both on a respiratory support unit and a critical care unit) and cost implications of subsequent resource utilisation up to 90

days follow-up measured by patient health resource use diaries
8.2. Cost-utility analysis using EQ-5D-5L quality-adjusted life years (QALYs) measured by questionnaire at 30 and 90 days post-randomisation
9. Responder analysis within the accelerated weaning group to identify predictors of success /failure

Overall study start date
01/04/2022

Completion date
30/06/2025

Eligibility

Key inclusion criteria
1. Clinical diagnosis of Exacerbation of Chronic Obstructive Pulmonary Disease, complicated by acute hypercapnic respiratory failure (pH <7.35 and $PaCO_2$ >6.5 kPa)
2. Age 35 years or over
3. Smoking history of 10 or more pack years
4. Low or medium risk Non-Invasive Ventilation (NIV) Outcomes score
5. Provision of acute NIV for 24 hours or longer
6. Correction of respiratory acidaemia
7. $PaCO_2$ <8 kPa, or $PaCO_2$ 8-9 kPa with at least a 20% fall in $PaCO_2$ from pre-NIV baseline value
8. Able to tolerate 60 minutes of unsupported breathing, confirmed by arterial blood gas (ABG)
9. Participants must be randomised within 24 hours of meeting the weaning criteria (based on the time of the qualifying ABG)

Participant type(s)
Patient

Age group
Mixed

Lower age limit
35 Years

Sex
Both

Target number of participants
164

Total final enrolment
164

Key exclusion criteria
1. Poor tolerance of NIV likely to limit adherence to protocol
2. Receiving home ventilation on admission, or planned referral for home ventilation on discharge
3. Inability to provide informed consent

4. Failure of another organ requiring level 2 or 3 organ support
5. Clinically significant pulmonary fibrosis
6. Metastatic cancer, advanced haematological malignancy, or other serious comorbidities, which may influence survival or decisions about ventilation within the time frame of the trial (3 months)

Date of first enrolment
19/09/2022

Date of final enrolment
02/04/2025

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Northumbria Specialist Emergency Care Hospital
Northumbria Way
Cramlington
United Kingdom
NE23 6NZ

Study participating centre
The Royal Victoria Infirmary
Queen Victoria Road
Newcastle upon Tyne
United Kingdom
NE1 4LP

Study participating centre
University Hospital of North Tees
Hardwick Road
Stockton-on-tees
United Kingdom
TS19 8PE

Study participating centre
Royal United Hospital
Combe Park
Bath

United Kingdom
BA1 3NG

Study participating centre
St James's University Hospital
Beckett Street
Leeds
United Kingdom
LS9 7TF

Study participating centre
Queens Medical Centre
Derby Road
Nottingham
United Kingdom
NG7 2UH

Study participating centre
Glenfield General Hospital
Groby Road
Leicester
United Kingdom
LE3 9QP

Sponsor information

Organisation
Northumbria Healthcare NHS Foundation Trust

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ResearchAndDevelopment@northumbria-healthcare.nhs.uk

Sponsor type
Hospital/treatment centre

Website
https://www.northumbria.nhs.uk/

ROR
https://ror.org/01gfeyd95

Funder(s)

Funder type
Government

Funder Name
Research for Patient Benefit Programme

Alternative Name(s)
NIHR Research for Patient Benefit Programme, RfPB

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Results will be shared with participants, presented at conferences and published in a high-impact peer-reviewed medical journal. The researchers will engage the relevant British Thoracic Society Specialist Advisory Groups, British Lung Foundation (reaching people with COPD).

Intention to publish date
31/12/2025

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study will be available upon request from the Chief Investigator Prof. Stephen Bourke (Stephen.Bourke@northumbria-healthcare.nhs.uk) from 6 months after the main papers related to this trial have been published, and provided the intended purpose and planned analysis are discussed and agreed in advance. Only anonymised data will be shared.

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 file	version 1.2	03/01/2023	02/01/2024	No	No
Statistical Analysis Plan	version 1.6	27/01/2025	07/02/2025	No	No
Statistical Analysis Plan	version 1.7	13/02/2025	21/02/2025	No	No