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Protocolised trial of invasive and non-invasive weaning off ventilation (The 'Breathe' Study)

Submission date	Recruitment status	[X] Prospectively registered
28/11/2012	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
29/11/2012	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
19/09/2019	Respiratory	

Plain English summary of protocol

Background and study aims
About 60,000 people each year in the UK become critically ill and require sedation and treatment with invasive mechanical ventilation given via a tube placed in the windpipe. Although initially lifesaving, invasive mechanical ventilation is associated with a number of complications including ventilator-associated pneumonia and prolonged requirements for sedatives with weakening of the leg, arm and breathing muscles. The longer a person requires invasive ventilation the poorer their chances of surviving. The process of liberating patients from invasive ventilation is referred to as weaning. Previous research has shown that implementing protocols for weaning can reduce the amount of time on a ventilator machine. There is also evidence that switching from invasive to non-invasive ventilation (also called mask ventilation) as an intermediate step in the weaning process may reduce the amount of time spent on the ventilator and complications. This study will compare protocolised invasive (tube) and non-invasive (mask) weaning strategies.

Who can participate?
Adult patients (male and female, age over 16 years) with respiratory failure who have received invasive ventilation for more than 48 hours (from the time of intubation) and fail a spontaneous breathing trial.

What does the study involve?
Patients are assessed daily for their readiness to commence weaning. Those ready for weaning are randomly allocated to either a protocolised weaning pathway that includes a period of mask ventilation or a protocolised pathway that does not include mask ventilation. The study measures the cost effectiveness and health benefits (time spent on a ventilator; survival, time spent in hospital including intensive care, complication rates) of each approach. The study also measures the impact of each approach on health-related quality of life using questionnaires.

What are the possible benefits and risks of participating?
Not provided.

Where is the study run from?
Warwick Clinical Trials Unit (UK).

When is the study starting and how long is it expected to run for?
January 2013 to July 2017

Who is funding the study?
National Institute for Health Research (NIHR) (UK)

Who is the main contact?
Mr Adam de Paeztron
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Study website
http://www.warwick.ac.uk/breathe

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
HTA 10/134/06, 13347

Study information

Scientific Title
Protocolised trial of invasive and non-invasive weaning off ventilation (The 'Breathe' Study): a pragmatic randomised controlled open multi-centre effectiveness trial

Acronym

BREATHE

Study objectives
The BREATHE trial will be a pragmatic, randomised, controlled, open, multi-centre, effectiveness trial to determine if the use of Non Invasive Ventilation (NIV) as an intermediate step in the protocolised weaning of patients off invasive ventilation is clinically and cost effective.

Patients with respiratory failure who have received invasive ventilation for more than 48 hours (from the time of intubation) and fail a spontaneous breathing test (SBT) will be randomised in a 1:1 ratio to invasive or non-invasive weaning strategies.

More details can be found at: https://www.journalslibrary.nihr.ac.uk/programmes/hta/1013406/#/

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee South Central Oxford C, First MREC approval date 05/10/2012, ref: 12/SC/0515

Study design
Pragmatic randomised controlled open multi-centre effectiveness 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 the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Topic: Generic Health Relevance and Cross Cutting Themes; Subtopic: Generic Health Relevance (all Subtopics); Disease: Critical Care

Interventions
The health technology being assessed is the use of NIV as an adjunct to protocolised weaning compared to protocolised weaning that does not include NIV following a failed spontaneous breathing trial.

Protocolised invasive weaning arm
The participant will be restarted on pressure supported ventilation at the previous settings. The level of pressure support (Psupp) will be titrated to achieve patient comfort and respiratory rate

<30 breaths min-1. Causes for distress / fatigue / weaning failure will be sought and corrective treatments initiated as appropriate. The patient will be reassessed every 2 hours. If there are no signs of distress / fatigue then the level of Psupp will be reduced by 2 cmH2O. This cycle will be repeated every two hours as tolerated. If at any stage the patient develops signs of distress / fatigue then they be will increased by 2 cmH2O. FiO2 will be titrated to maintain SaO2 > 90%. A further SBT will take place each morning. This cycle will continue until the patient has either been extubated (due to passing the SBT or tolerating Psupp 5 cmH2O) or a tracheostomy is performed.

This active weaning protocol will occur between 8am-10pm. Unless the participant develops signs of fatigue or distress, ventilator settings will not be changed overnight.

Protocolised non-invasive arm
Participants allocated to the NIV arm will be extubated and immediately provided with NIV with an equivalent level of pressure support and PEEP to the ventilator settings prior to extubation. After 2 hours, if no signs of distress / fatigue occur then the NIV interface will be removed and the participant will undergo a self-ventilation trial with supplemental oxygen (equivalent to the previous FiO2) being provided via a standard oxygen mask.

If no signs of distress or fatigue develop during the self-ventilation trial the patient will continue receiving unsupported ventilation with inhaled oxygen being provided as required. If the participant subsequently develops signs of distress or fatigue, NIV will be re-started (as below). Otherwise the participant will continue with unsupported self-ventilation. FiO2 will be titrated to maintain SaO2 > 90%.

If signs of distress or fatigue develop NIV will be re-instated at the previous settings. The level of pressure support (Psupp) will be titrated to achieve participant comfort and a respiratory rate < 30 breaths min-1. Causes for distress / fatigue / weaning failure will be sought and corrective treatments initiated as appropriate. The participant will be reassessed every 2 hours. If there are no signs of distress / fatigue then a further trial of self-ventilation will be commenced as described above.

This active weaning protocol will occur between 8am-10pm. Unless the participant develops signs of fatigue or distress, ventilator settings will not be changed overnight.

NIV will be withdrawn when the participant tolerates 12 hours unsupported spontaneous ventilation.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Time from randomisation to liberation from ventilation

Secondary outcome measures
Efficacy:
1. Mortality at 30, 90 and 180 days
2. Duration of IMV and total ventilator days (invasive and non-invasive ventilation)

3. Time to meeting ICU discharge criteria (defined as no further requirement for level 2/3 care)
4. Proportion of patients receiving antibiotics for presumed respiratory infection and total antibiotic days
5. Re-intubation rates (protocolised end-point and actual event)
6. Tracheostomy

Safety:
1. Adverse events
2. Serious adverse events

Patient focused outcomes:
Health-related quality of life, measured using EuroQol, EQ-5D, SF12 at baseline (estimated), 3 and 6 months

Overall study start date
01/01/2013

Completion date
31/07/2017

Eligibility

Key inclusion criteria
1. Male and female, age > 16 years
2. Patients with respiratory failure who have received invasive ventilation for more than 48 hours (from the time of intubation)
3. Fail a spontaneous breathing trial (SBT)
4. Provision of written informed consent

The trial inclusion criteria will be adult patients with respiratory failure who have received invasive ventilation for more than 48 hours (from the time of intubation) and fail a SBT. We will not include patients who require shorter periods of invasive ventilation or those who pass the SBT as this group are typically rapidly weaned and have good clinical outcomes.

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
Revised sample size 364; UK sample size 364

Total final enrolment
364

Key exclusion criteria

1. Presence of tracheostomy
2. Profound neurological deficit
3. Any absolute contraindication to NIV
4. Home ventilation prior to ICU admission
5. Decision not to re-intubate or withdrawal of care anticipated
6. Further surgery / procedure requiring sedation planned in next 48 hours
7. Previous participation in the trial

Date of first enrolment
01/01/2013

Date of final enrolment
04/10/2016

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Warwick Medical School
Coventry
United Kingdom
CV4 7AL

Sponsor information

Organisation
Heart of England NHS Foundation Trust (UK)

Sponsor details
3 Bordesley Green East
Bordesley Green
Birmingham
England
United Kingdom
B9 5SS

Sponsor type
Hospital/treatment centre

Website
http://www.heartofengland.nhs.uk/

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal one year after overall trail end date.

Intention to publish date
31/12/2018

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date

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?
Results article	results	13/11/2018		Yes	No
Results article	results	01/09/2019	19/09/2019	Yes	No