ISRCTN14092678 https://doi.org/10.1186/ISRCTN14092678

Nasal high-flow oxygen therapy after cardiac surgery

Submission date 14/04/2020	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [X] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 13/05/2020	**Overall study status** Completed	
Last Edited 21/05/2025	**Condition category** Surgery	

Plain English summary of protocol

Background and study aims
Patients with pre-existing lung conditions undergoing heart surgery are at higher risk of complications after surgery such as chest infection or pneumonia. They may need a tight-fitting mask to help them breathe and ensure that enough oxygen gets into their blood and carbon dioxide is removed. This treatment is costly, labour intensive and can be uncomfortable. Treatment for lung complications can lead to a prolonged hospital stay or even death. Recently, there has been increased interest in the use of high-flow nasal therapy (HFNT) after cardiac surgery. High-flow nasal therapy (HFNT) provides warmed humidified oxygen (air that is warmed and contains some moisture) and has been shown to assist breathing and improve patient recovery. HFNT is comfortable during use and may be even more comfortable than standard treatment with dry oxygen via a face mask or nasal prongs. Without a tight-fitting mask, patients can eat normally and speak freely. In light of this, a study recently investigated whether high-risk patients with certain lung conditions (asthma, chronic obstructive pulmonary disease) or a risk factor for postoperative lung complications (obesity, recent chest infections or heavy smoking), would benefit from routine administration of high-flow nasal therapy immediately after cardiac surgery. The study showed that when compared with standard care, the use of HFNT significantly reduced hospital length of stay (by 29%) and was associated with fewer re-admissions to the intensive care unit. This was the first randomised trial to examine the effect of high-flow nasal therapy compared to standard dry oxygen via nasal prong, on patient-relevant outcomes (length of hospital stay), after open-heart surgery in patients at high risk of postoperative lung complications. The researchers presented the study results to patients who participated in this first trial and both clinicians and participants agreed that it is extremely important to test whether the results can be replicated in a large multicentre study. This study will expand the first trial into nine other UK hospitals (ten hospitals in total including Royal Papworth Hospital), seven Australian hospitals and one hospital in New Zealand, in order to see if the positive findings can be repeated and whether HFNT should become routine in this patient group after cardiac surgery.

Who can participate?
Patients aged 18 or over who are scheduled to undergo open-heart surgery conducted on

cardiopulmonary bypass and have one or more risk factors (e.g. chronic lung disease [COPD], asthma, current or recent smoker, recent chest infection, obesity) for developing breathing complications after the operation.

What does the study involve?
To assess the effect of HFNT the researchers will be recruiting a minimum of 1280 participants from ten UK hospitals, seven Australian hospitals and one hospital in New Zealand, and randomly allocating them to receive high-flow nasal therapy or standard oxygen therapy. Before their surgery, participants will be asked to complete two quality-of-life questionnaires and a questionnaire collecting information about where they live, health service use 1 month before surgery and current medications. On the day of surgery, the surgical procedure will go ahead as usual and it will be during surgery that allocation to treatment is done. As participants are woken from surgery, the intensive care nurses and doctors will give the allocated therapy for a minimum of 16 hours after surgery (with a total of 1 hour off treatment allowed for any required transfers around the hospital and/or physio mobilisation). Upon discharge from hospital, participants will be asked to maintain a location and medication diary and to complete the same questionnaires as before surgery, on three further occasions. Participants will be followed up by the Royal Papworth Hospital research team at 30 and 90 days after surgery.

What are the possible benefits and risks of participating?
High-flow nasal therapy is an established therapy which is proven to be safe and effective in a variety of clinical settings. If, after surgery, participants require more support with their breathing, the clinical team will always have the ability to give what they feel is most beneficial. High-flow nasal therapy does generate some low-level noise and participants may feel hot whilst wearing the device due to the warmed humidified oxygen. If a participant starts to feel too hot, a nurse or doctor can decrease the temperature of the oxygen slightly or provide a fan to cool them down. There are no direct personal benefits for participating in the study; however, participants could help a future generation of patients make better-informed choices about their treatment. For participants allocated to high-flow nasal therapy, they may experience benefits in terms of making breathing easier, reducing the chances of their lungs getting blocked by secretions and reducing the chances of picking up a chest infection (e.g., pneumonia). This may mean participants feel better quicker after surgery.

Where is the study run from?
1. Royal Papworth Hospital (UK)
2. Curtin University (Australia)
3. Auckland City Hospital (New Zealand)

When is the study starting and how long is it expected to run for?
January 2019 to September 2024

Who is funding the study?
1. National Institute for Health Research, Health Technology Assessment (NIHR HTA) (UK)
2. Green Lane Research and Education Fund (New Zealand)
3. Medical Research Future Fund International Clinical Trial Collaboration (MRFF ICTC) (Australia)

Who is the main contact?
The NOTACS Team
papworth.notacsstudy@nhs.net

Contact information

Type(s)
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
278290

ClinicalTrials.gov (NCT)
NCT05308719

Protocol serial number
CPMS 45298, IRAS 278290

Study information

Scientific Title
Nasal high-flow oxygen therapy after cardiac surgery (NOTACS) study: effect of high-flow nasal therapy on patient-centred outcomes in patients at high risk of postoperative pulmonary complications after cardiac surgery: a multicentre randomised controlled trial

Acronym
NOTACS

Study objectives
To determine if prophylactic use of HFNT (for a minimum of 16 hours after tracheal extubation) is clinically- and cost-effective up to 90 days after surgery, for adult patients undergoing cardiac surgery with cardiopulmonary bypass who are at high risk of postoperative pulmonary complications.

Ethics approval required
Ethics approval required

Ethics approval(s)
1. approved 24/04/2020, Yorkshire & The Humber - Leeds West Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ, United Kingdom; +44 (0)207 1048053; leedswest.rec@hra.nhs.uk), ref: 20/YH/0133 (for UK sites)

2. approved 03/09/2021, South Metropolitan Health Service Human Research Ethics Committee (SMHS, Level 2, Education Building, Fiona Stanley Hospital, 14 Barry Marshall Parade, Murdoch, 6150, Australia; +61 (0)861522064; SMHS.HREC@health.wa.gov.au), ref: RGS0000004935 (for Australian sites)

3. approved 12/10/2021, Health and Disability Ethics Committees (133 Milesworth Street, Thorndon, Wellington , 6011, New Zealand; -; hdecs@health.govt.nz), ref: 21/STH/213 (for New Zealand site)

Study design
Randomized; Interventional; Design type: Treatment, Device

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Postoperative pulmonary complications after cardiac surgery

Interventions
The study is an adaptive, multicentre, parallel-group, randomised controlled clinical trial with embedded cost-effectiveness analysis comparing the use of high-flow nasal therapy (HFNT), to standard oxygen therapy for a minimum of 16 hours after tracheal extubation (added 19/10/2023: with a total of 1 hour off treatment allowed for any required transfers around the hospital and/or physio mobilisation), in patients at high risk of respiratory complications following cardiac surgery. Participants will be recruited over 3 years. Potential participants scheduled for elective or urgent first-time or re-do cardiac surgery (coronary artery bypass grafting (CABG), valve surgery or both) will be screened for eligibility. Written informed consent will be obtained from all research participants prior to any study-related procedures. Baseline quality of life questionnaires will be completed. Randomisation will be performed while the participant is undergoing surgery. Participants will be randomly assigned to receive either HFNT or standard oxygen therapy using an online tool (provided by Sealed Envelope). Randomisation will be stratified by centre. After cardiac surgery, participants will be transferred sedated and with their trachea intubated to the post-surgical recovery area. This may be an Intensive Care Unit, High-Dependency Unit or specific Recovery Unit as per local practice. Once participants fulfil the standard agreed protocol [minimal bleeding via chest drains; temperature >36°C; stable cardiovascular function; neuromuscular block worn off or reversed; sedation stopped; patients responsive to command and successful trial without mechanical ventilation (defined as oxygen saturation ($Sp0_2$)> 93% with inspired oxygen less than or equal to 60%)], they will then be extubated according to the agreed Trial Extubation Protocol (Appendix 2 in the protocol) and will receive either HFNT or standard oxygen therapy for a minimum of 16 hours according to their randomised allocation (added 19/10/2023: with a total of 1 hour off treatment allowed for any required transfers around the hospital and/or physio mobilisation). Participants will be transferred to the surgical ward as per local practice and will be assessed at least every 24 hours as per local practice – if $Sp0_2$ > 93% on air and RR < 20, then HFNT or standard oxygen will be discontinued. If $Sp0_2$ <93% or RR > 20, then HFNT or standard oxygen will be continued for a further 24 hours then the participants will be re-assessed every 24 hours. If a participant deteriorates during HFNT or standard oxygen therapy, then the agreed Trial Escalation of Respiratory Therapy Protocol will be followed (Appendix 3 in the protocol). At discharge participants will complete the quality of life questionnaires again and be given a patient location and medication diary to complete up to 90 days after surgery. Participants will be asked to record any changes to their living location and also any changes to their medication after surgery. Participants will be also followed up by the central clinical trials unit staff and contacted at 30 and 90 days to collect outcome data and complete questionnaires (all by internet or phone, no additional visits to the hospital necessary). Participants will be asked at the time of recruitment if they would like to use online questionnaires or telephone to collect data. GPs or their receptionists will be contacted by the central clinical trials unit staff to verify the data collected. Participants will normally attend back to the hospital for surgical follow-up at 6-8 weeks independently of the trial.

Intervention Type
Other

Primary outcome(s)

Current primary outcome measures as of 21/05/2025:
1. Number of days at home without additional support in the first 90 days after surgery, measured by the Patient Location and Medication Diary at 90 days
2. Health economic analysis to estimate the incremental cost-effectiveness and cost-utility of HFNT versus standard oxygen therapy, measured using Patient and Family Resource Use Questionnaires at baseline and 90 days

Previous primary outcome measures as of 15/04/2021:
1. Number of days at home in the first 90 days after surgery, measured by the Patient Location and Medication Diary at 90 days
2. Health economic analysis to estimate the incremental cost-effectiveness and cost-utility of HFNT versus standard oxygen therapy, measured using Patient and Family Resource Use Questionnaires at baseline and 90 days

Previous primary outcome measures:
1. Number of days at home in the first 90 days after surgery, measured by the Patient Location and Medication Diary at 90 days
2. Health economic analysis to estimate the incremental cost-effectiveness and cost-utility of HFNT versus standard oxygen therapy, measured using Patient and Family Resource Use Questionnaires at baseline, discharge, 30 and 90 days

Key secondary outcome(s))

Current secondary outcome measures as of 15/04/2021:
The following are exploratory secondary outcomes of the study:
1. Estimates of the incremental cost-effectiveness and cost-utility of HFNT versus standard oxygen therapy, calculated by a health economic analysis at 30 days
2. Mortality measured by the incidence of death during primary hospital admission and at patient follow-up at 30 and 90 days
3. Incidence of postoperative pulmonary complications measured using medical notes during primary admission to hospital
4. ICU re-admission rate measured using the in-patient diary eCRF at any time during primary hospital admission
5. Length of ICU stay (days) measured using the in-patient diary eCRF during primary hospital admission
6. Length of hospital stay (days) measured using the in-patient diary eCRF during primary hospital admission
7. Incidence of stroke measured during primary hospital admission and at patient follow-up at 30 and 90 days
8. Incidence of sepsis measured during primary hospital admission and at patient follow-up at 30 and 90 days
9. Incidence of myocardial infarction measured during primary hospital admission and at patient follow-up at 30 and 90 days
10. Oxygenation measured by ROX Index (defined as $Sp0_2/Fi0_2$ to respiratory rate ratio) at 2, 6, 12, 24 and 48 hours post-extubation
11. Patient-reported outcomes measured using the EQ-5D-5L questionnaire at baseline, discharge, 30 and 90 days
12. Patient-level of assistance needed with activities of daily living, measured using the BARTHEL questionnaire at baseline, discharge, 30 and 90 days
13. Quality of survival measured using EQ-5D-5L Quality Adjusted Life Years (QALYs) at baseline, discharge, 30 and 90 days
14. Health service and resource use measured using Patient and Family Resource Use Questionnaires at baseline, discharge, 30 and 90 days

15. Incidence of readmission to hospital rate, measured using the in-patient diary eCRF during primary hospital admission

Previous secondary outcome measures:
The following are exploratory secondary outcomes of the study:
1. Estimates of the incremental cost-effectiveness and cost-utility of HFNT versus standard oxygen therapy, calculated by a health economic analysis at 30 days
2. Mortality measured by the incidence of death reported from patient follow-up and medical records at 30 and 90 days.
3. Incidence of postoperative pulmonary complications measured using medical notes during primary admission to hospital
4. ICU re-admission rate measured using the in-patient diary eCRF at any time during primary hospital admission
5. Length of ICU stay (days) measured using the in-patient diary eCRF during primary hospital admission
6. Length of hospital stay (days) measured using the in-patient diary eCRF during primary hospital admission
7. Incidence of stroke measured from patient follow-up and medical records at 30 and 90 days
8. Incidence of sepsis measured from patient follow-up and medical records at 30 and 90 days
9. Incidence of myocardial infarction measured from patient follow-up and medical records at 30 and 90 days
10. Oxygenation measured by ROX Index (defined as $Sp0_2/Fi0_2$ to respiratory rate ratio) at 2, 6, 12, 24 and 48 hours post-extubation
11. Patient-reported outcomes measured using the EQ-5D-5L questionnaire at baseline, discharge, 30 and 90 days
12. Patient level of assistance needed with activities of daily living, measured using the BARTHEL questionnaire at baseline, discharge, 30 and 90 days
13. Quality of survival measured using EQ-5D-5L Quality Adjusted Life Years (QALYs) at baseline, discharge, 30 and 90 days
14. Health service and resource use measured using Patient and Family Resource Use Questionnaires at baseline, discharge, 30 and 90 days
(added 14/04/2021)
15. Incidence of readmission to hospital rate, measured using the in-patient diary eCRF during primary hospital admission

Completion date
17/09/2024

Eligibility

Key inclusion criteria
Current inclusion criteria as of 19/10/2023:
1. Aged 18 years or over
2. Undergoing any elective or urgent first-time or redo cardiac surgery performed on cardiopulmonary bypass
3. Have one or more clinical patient-related risk factor for postoperative pulmonary complications (COPD, asthma, lower respiratory tract infection in last 4 weeks as defined by use of antibiotics, body mass index >=35 kg/m², current (within the last 6 weeks) heavy smokers (>10 pack years)

Previous inclusion criteria from 05/07/2023 to 19/10/2023:
1. Aged 18 years or over
2. Undergoing elective or urgent first-time or redo cardiac surgery performed on cardiopulmonary bypass
3. Have one or more clinical patient-related risk factor for postoperative pulmonary complications (COPD, asthma, lower respiratory tract infection in last 4 weeks as defined by use of antibiotics, body mass index >=35 kg/m², current (within the last 6 weeks) heavy smokers (>10 pack years)

Previous inclusion criteria:
1. Aged 18 years or over
2. Undergoing elective or urgent first-time or redo cardiac surgery (CABG, valve surgery, surgery on the aorta or any combination)
3. Have one or more clinical patient-related risk factors for postoperative pulmonary complications (COPD, asthma, lower respiratory tract infection in last 4 weeks as defined by the use of antibiotics, body mass index >=35 kg/m², current (within the last 6 weeks) heavy smokers (>10 pack years)

For the purposes of the study, the following definitions apply:

Asthma is a disease characterized by recurrent attacks of breathlessness and wheezing, and patients will have been prescribed medication by inhalers or nebulisers (either bronchodilators or steroids).

Chronic Obstructive Pulmonary Disease (COPD) is an umbrella term used to describe chronic lung diseases that cause limitations in lung airflow. The more familiar terms 'chronic bronchitis' and 'emphysema' are no longer used but are now included within the COPD diagnosis. The most common symptoms of COPD are breathlessness, or a 'need for air', excessive sputum production, and a chronic cough. Patients suitable for the NOTACS study will have been prescribed medication by inhalers or nebulisers (either bronchodilators or steroids).

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
1280

Key exclusion criteria

1. Requiring home oxygen therapy
2. Deep hypothermic circulatory arrest planned
3. Contraindication to HFNT, e.g. nasal septal defect
4. Requirement for home respiratory support (including: CPAP, BiPAP)
5. Requiring emergency cardiac surgery defined as surgery required within 24 hours of the decision to operate
6. Patients not fluent in English

Date of first enrolment
07/10/2020

Date of final enrolment
19/06/2024

Locations

Countries of recruitment
United Kingdom

England

Scotland

Wales

Australia

New Zealand

Study participating centre
Royal Papworth Hospital NHS Foundation Trust
Papworth Everard
Cambridge
United Kingdom
CB23 3RE

Study participating centre
University Hospitals Of Leicester NHS Trust
Leicester General Hospital
Gwendolen Road
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Study participating centre
Guy's and St Thomas' NHS Foundation Trust
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London
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Study participating centre
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Study participating centre
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Study participating centre
University Hospitals Birmingham NHS Foundation Trust
Queen Elizabeth Hospital
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B15 2GW

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

Study participating centre
NHS National Waiting Times Centre Board
Golden Jubilee National Hospital
Agamemnon Street
Clydebank
United Kingdom
G81 4DY

Study participating centre
Cardiff & Vale University Local Health Board
University Hospital of Wales
Health Park
Cardiff
United Kingdom
CF14 4XW

Study participating centre
Auckland City Hospital
Park Road
Grafton
Auckland
New Zealand
1023

Study participating centre
Fiona Stanley Hospital
11 Robin Warren Drive
Murdoch
Australia
WA 6150

Study participating centre
St John of God Hospital
12 Salvado Road
Subiaco
Australia
WA 6008

Study participating centre
The Townsville University Hospital
100 Angus Smith Drive

Douglas
Australia
QLD 4814

Study participating centre
The Prince Charles Hospital
Rode Rd
Chermside
Australia
QLD 4032

Study participating centre
Royal North Shore Hospital
Reserve Road
St Leonards
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NSW 2065

Study participating centre
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Melbourne
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VIC 3004

Study participating centre
The University Hospital Geelong, Barwon Health
Bellerine Street
Geelong
Australia
VIC 3220

Sponsor information

Organisation
Royal Papworth Hospital NHS Foundation Trust

Organisation
Curtin School of Population Health

Funder(s)

Funder type
Government

Funder Name
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC); Grant Codes: NIHR128351

Funder Name
Green Lane Research and Educational Fund

Alternative Name(s)
Green Lane Research and Education Trust, GLREF

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
New Zealand

Funder Name
Medical Research Future Fund International Clinical Trial Collaboration (MRFF ICTC) (Australia)

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Melissa Duckworth (papworth.notacsstudy@nhs.net). This will be anonymised data and will only be released after the publication of the monograph.

IPD sharing plan summary
Available on request

Study outputs

	Date	Date	Peer	Patient-

Output type	Details	created	added	reviewed?	facing?
Protocol article		28/03/2022	13/07/2023	Yes	No
Protocol article	Economic evaluation protocol and analysis plan	28/01/2025	31/01/2025	Yes	No
HRA research summary			28/06/2023	No	No
Interim results article		20/08/2022	22/08/2022	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Statistical Analysis Plan		20/08/2022	13/07/2023	Yes	No
Statistical Analysis Plan		06/11/2024	12/11/2024	No	No